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ROLLIN HOWARD STEVENS

AN ANNIVERSARY CHRONICLE OF HIS USEFUL LIFE

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ONE of the most active and vigorous figures in the practice of American radiology to-day is that of Dr. Rollin Stevens, who now reaches the age of three score years and ten prophetically signalized in Scriptural writ, and whose enthusiastic, sedulous, and forthright individuality, crystallized in the service of mankind and polished by the gentle contact of each passing year, continues to reflect from its many facets his faith in his work and in himself in the doing of it, as well as the joy of fulfilment which the realization of his life's ideals has assured to him.

Rollin Stevens is a native of Canada, born of sturdy Anglo-Saxon and Celtic stock into the best traditions of the great Dominion at Blenheim, Province of Ontario, in early January of the year 1868. The eldest son of Nathan Howard and Ada Jane (Burk) Stevens, he lived with his parents at his birth-place until five years old, when the family removed to the far western community of Pilot Hill, California, in the placer-mining district of the Sierras. His father remained in California but a relatively short time, ultimately leading back his household to the Canadian village of Blenheim and later, in 1880, to the larger town of Chatham, Ontario. By reason of his seniority in a family group of nine children, eight of whom were boys, the youthful shoulders of this lad carried, as they grew, more than the usual weight of the responsibility imposed by the duties of home life and the care of those younger than he. Notwithstanding his ardent participation in the various sports and pastimes, especially those of winter, wherein Canadian youth habitually excel, through this salutary family training young Stevens developed a sense of obligation and accountability, acquired a fondness for hard work and formed the sound attributes of character which have ever identified all phases of his life's endeavor.

By the time he was eighteen years old, Stevens had matriculated at the University of Toronto in preparation for the academic degree and subsequent study of the Law in accordance with parental plan, but during the year 1886 he was induced by a young friend of about his own age[1] to enter the Homoeopathic Medical College of the University of Michigan, from which he was graduated in 1889. Throughout the course of his later years in medical school his extra-curricular activities were increased—in junior year as Secretary of the Hahnemannian Society and in

[1] Now Dr. Duncan I. Sinclair, of Woodstock, Ontario.

senior year as its President and also President of the Homoeopathic Branch of the Students' Christian Association. During the course of his senior year he was also Senior Assistant to the Professor of Surgery. His summer holidays were spent as coadjutor in the office of a private practitioner of St. Thomas, Ontario, where his training profited by the practical experience afforded him. While yet a student at Ann Arbor, Stevens took advantage of the opportunity to present himself for the examinations of the Medical Council of Ontario, which he duly passed, thus qualifying himself for the practice of medicine in his native Dominion of Canada, should the occasion arise.

Upon his graduation from medical school, young Doctor Stevens fully determined to enter into practice in one of the (then) more recently founded Canadian communities, the city of New Westminster in British Columbia, but, hearing of an approaching competitive examination for the position of intern at The Grace Hospital, Detroit, he offered himself as a candidate. No doubt the divers interests of his undergraduate medical course and the moderate responsibilities attaching to them did much to develop a naturally active mind at its formative period, for we are told by a surgical colleague who was the first House Surgeon at The Grace Hospital[2] in reference to this examination, that " . . . Dr. Stevens received the appointment. Dr. Sterling, . . . who was the Chairman of the Examining Committee, said that the alertness of Dr. Stevens' mind as much as the results of the examination papers influenced them in the decision. That alertness seems to me to have been a characteristic of Dr. Stevens ever since." As the resident staff of The Grace Hospital consisted, at that day, of but one man, Stevens' duties were especially arduous during the first eight months of his appointment, after which the number of house-officers was increased to two.

Doctor Stevens' internship at The Grace Hospital was completed late in the year of 1891. It was followed by a journey with his father to California, by way of the Canadian Pacific Railway. Impressed by the opportunity for post-graduate study at the recently established Leland Stanford, Jr., University, the young physician finally succeeded in inducing his fiancée, Dr. Mary Ella Thompson, to accompany him there on a honeymoon journey. Doctor Thompson was a young graduate in Arts and in Medicine, also a Canadian, whom he had met at Ann Arbor and who had opened an office in Detroit in the Autumn of 1889, just before he had decided to take the examination for The Grace Hospital. Accordingly they were married in March of 1892, journeyed West, and commenced post-graduate work at Palo Alto in physiology and pathology, which was continued until autumn, when they returned to Detroit to open offices in their domicile on High Street, West. With this wedding journey into the far West began a consistently happy companionship that has been ever fortified by a compatibility of tastes derived from a unifying analogy of educational equipment, and exceptionally blessed by mutual affection and sympathy steadily augmented with the passing years.

His entry into private practice was an experience not wholly new to young Doctor Stevens. He had already acted as *locum tenens* for medical colleagues of his who were at work in various towns of Ontario, for which his previously acquired license to practise within the Dominion stood him in good stead. Once established in Detroit, he immediately identified himself with the clinical activities at The Grace Hospital, and was placed on the Clinical Staff in Gynecology. When, later, he received his appointment to the regular Staff, he became successively pathologist, surgeon, and gynecologist during the period from 1892 to 1904. His thorough pathological experience, thus early acquired and amplified by additional work in weekly periods at Ann Arbor, afforded him the *sine qua non* for his fu-

[2] Dr. Stephen H. Knight, *personal communication.*

DR. ROLLIN HOWARD STEVENS

(1) In 1885. The year preceding his entrance to the University; (2) In 1889. At the time of his graduation; (3) In 1890. When an intern at The Grace Hospital; (4) In 1899. When in general practice in Detroit; (5) In 1903. At the time of his visit to Copenhagen; (6) In 1910. When teaching at the Detroit College of Medicine; (7) In 1914. At the outbreak of the Great War; (8) In 1917. At the time of America's entry into the War; (9) Doctor Stevens at the present day.

ture activity in the broad and ever broader fields which were spread before him as the first years of the Twentieth Century approached. The colorful history of his multiple and diverse labors at The Grace Hospital is the ample record of the fruition of the mental alertness originally noted by his internship examiners years ago, and as clearly manifested to-day in the "physical and mental youthfulness and agility" —as one of his biographers puts it—that are still his.

Always keenly alive to each fresh advance in scientific progress, whether or not related to his work of the moment, Doctor Stevens had shared the general intense interest among scholars created by Röntgen's *Preliminary Communication*, "On a New Kind of Rays," but perhaps he was attracted more than many others by the results reported soon after this by Professor Finsen, of Copenhagen, in the light treatment of variola and especially of dermal cancer and tuberculosis. As time passed thereafter, his acute sense of justice rebelled at the implications involved in the production and exploitation, especially in America, of so-called Finsen therapeutic apparatus from which the results obtained were most disappointing. Desiring, as he shortly afterward wrote, "to protest against the common practice of denominating as Finsen lamps any kind of a phototherapeutic lamp, the construction of which may involve only a few, or none, of the principles enunciated by Finsen," he journeyed by rough passage to Copenhagen in December of 1902 to investigate for himself and to evaluate to his own satisfaction the Finsen method of treatment. At the Finsen Institute Stevens spent many months as student and observer, and was given all possible clinical opportunities for his work. He ultimately returned with the accurate information equally available to any of his countrymen taking equivalent pains to investigate, although many others, visiting Copenhagen on but a short mission of investigation and brief instruction, relinquished in the disappointment of ineptitude all subsequent use of the Finsen lamp. On his return Stevens reported, and reiterated in a series of communications which constitute the earliest of his writings on radiological matters, that the secret of the Finsen treatment lies in the use of the highly refrangible blue and violet rays *supported and enhanced* in their effect by the addition of the ultra-violet. In the same series of papers he analyzed the structural shortcomings of a number of lamps produced prior to 1904 and purported to possess the same therapeutic effect as the Finsen apparatus. This persistent investigation at distinct personal sacrifice, and honestly accurate exposition of a truly beautiful and effective means of curing "superficial skin diseases that are suitable for it," had definite effect in dispelling "much misunderstanding as to the nature of the true Finsen light treatment and as to what it will accomplish," but even greater influence in arresting the manufacture of spurious apparatus offered to the unsuspecting practitioner for what it was not.

This pilgrimage of quest to the Finsen Institute may fairly be said to mark a distinct turning-point in the career of Dr. Rollin Stevens. He saw an opportunity to clarify an uncertain situation regarding a conceivably excellent measure in danger of undeserved misrepresentation, and seized it. The untoward influence of such obloquy atrophied and died in the face of the clinical results obtained from the veritable Finsen process in his hands at Detroit, or in the hands of those whom he had trained to have patience enough to employ it accurately.

In Denmark, Stevens saw enough of the beneficial effects of well-ordered phototherapy to revive within him a long-latent interest in dermatological problems. Before his return to Detroit he visited the clinics of Lassar and Joseph in Berlin, of Neumann in Vienna, of Unna in Hamburg, and of Sequeira in London. At the same time, the clinical possibilities of roentgen therapy and of radium therapy had had their day of dawning and were rapidly de-

veloping. A vast new field was spread before the clear vision of Rollin Stevens and on his arrival at the scene of his long and varied professional labors, he determined to confine his endeavor to the practice of dermatology and radiology.

To this end, Doctor Stevens forthwith equipped his offices with Finsen apparatus of the true Copenhagen type, for roentgen rays in the form of the static machine and for the therapeutic application of the high-frequency current. He was transferred to the Dermatological Staff of his hospital and in 1904 formally appointed Dermatologist and Roentgenologist as well as Lecturer on Dermatology to the Homoeopathic Medical College of the University of Michigan. The sincerity of his belief in the future of roentgen therapy, as well as the continued evidence of his thorough honesty of purpose, convinced the hospital authorities of their need of roentgen apparatus adequate to his purposes and theirs, for his use and under his responsible control. But the winning of this concession was no easy accomplishment; a true picture, indeed, of the typical experience of the conscientious early pioneer in radiology and, as in the case of many another in the same field, it was by no means the end of the difficulties in his path. It is related by his most steadfast supporter and at the same time his most just critic,[3] that "for years he was almost alone in [his] recognition of the great value of both x-ray and radium in skin and cancer work. Many times he returned to his home completely heartsick after reading a carefully prepared paper on the subject, only to have it almost completely ignored while the loud acclaim went to someone who described a new method or posture for a roentgenogram of the stomach."

In the Summer of 1903, Doctor Stevens obtained his first radium from the Curie laboratory in Paris, and thus, it is reported, he was the first practising physician west of New York to employ radium therapeutically. Consequently he was of the American pioneer group of such men as Abbe, Williams, and Robarts who early investigated practically its curative powers. In 1905 he made his first recorded contribution to the literature of radium. With characteristic loyalty to his ideals of truth and justice, he scrutinized, and promptly evaluated at their true worth, the reports prevalent at that day concerning water and other substances made secondarily radioactive for alleged therapeutic purposes. It is difficult to conceive of one who, through his own moral fiber, could have been a more worthy champion of intellectual honesty in counteraction against not only the reckless hyper-enthusiasm but also the upstart charlatanism which this period brought forth.

Stevens fought this situation for years. Writing in 1914 on "Progress in Radiotherapy," in the spirit of complete equity typical of him he deals with his failures as freely as with his successes in all forms of radiotherapeusis, and attempts definitely to stabilize this tendency toward unconsidered optimism arising from too hasty observation. Regarding the use of the gamma rays of radium, he records these temperate words of caution:

> "We must not forget that in secondary growths we undoubtedly have cancer widely spread in the organism—in the spine or other bones quite early in a large proportion of cases —so that while, in the treatment of a small visible or palpable nodule in the axilla or supraclavicular region, a small tube or plaque of radium may cause the nodule to disappear, it has had no very real effect upon the disease.
>
> "I emphasize this point because at least two cases of secondaries after breast amputation have recently come to my notice where just this sort of treatment has been followed, and twenty to thirty thousand dollars' worth of radium was applied to visible nodules by men of standing *while hope was held out.* This will soon bring radium into disrepute."

The reaction which Stevens thus sagely prognosticated as the certain result of the disillusion and disappointment to follow the inevitably unfavorable outcome of such ill-ordered treatment was, indeed,

[3] Dr. Mary Thompson Stevens, *personal communication.*

soon to appear. During the same year of 1914 in which this unpretentious report and far-sighted prophecy were written, and *sixteen years* after the discovery of radium, the following editorial appeared in a medical journal of wide circulation under the caption "The New Quackery." Its quotation here is justified only on expository grounds, in order that the radiologist of to-day may realize the type of adverse criticism to which early radiology was subjected in a spirit born either of temporary clinical disappointment or of no clinical experience at all, as well as the magnitude of the task in rebuttal set before Stevens and other pioneers of the same fiber:

"Radium is the Philosopher's Stone in its newest form. . . . What the alchemists and necromancers eagerly sought our new philosophers have found. . . . The profession of Medicine is . . . now disposed to ask of the philosopher not what he says but what he can prove. . . . Any new half-truth in Medicine is quickly seized upon with enthusiastic ignorance to benefit the sick, or with cunning design to impose upon the credulous. All quackery does not lie outside the boundaries of the medical profession, and it is hard to distinguish between credulity, pretence and charlatanism.

"For the moment sera are enjoying a respite. . . . Their place is now occupied by radium, and reputations of a kind are being erected upon it. The moment is well chosen. The public mind is blinded by the glamour of the emanations which issue from this substance, and no discovery was ever made which was not instantly seized upon for therapeutic purposes. . . . All that can be said at the moment is that the emanations from this metal do exert some effect upon cell activity; but the same is true of the ultra-violet rays or even of light itself. Already reports of bad omen are coming in of healthy tissue destroyed and of connective-tissue cells being stimulated into a sarcomatous growth. . ."

The effect of immaturely considered dogma could be counteracted in but one way—by further observation and further experimentation and study. The span of Stevens' career from that day to this has seen prodigious and unremitting advance in all forms of radiotherapeusis, and we move forward with giant strides.

It was six years before this extensive report of 1914, on the subject of radiotherapeutic progress to that date, that Doctor Stevens suffered a temporary but serious interruption of his usually excellent health, which followed the exertion and exposure attending a late autumn journey by canoe into the back country of northern Ontario with one of his colleagues. That he might regain his normal strength, a sea voyage was recommended. So, in the Spring of 1909 he went to Europe for recreation and study. In London, he visited the laboratory of Sir Almroth Wright to investigate further the matter of opsonic therapy. With his habitual eagerness to prove to his own satisfaction the real value of each new method of treatment applicable to cutaneous disease, Stevens had previously contributed a preliminary report on his own experience with opsonic therapy in disorders of the skin and, later, a more complete exposition based on eight months' experience with it. These were followed by a paper on the general subject of bacterial inoculations which appeared in the literature of 1909, possibly a result of his London visit. In Paris, on this same tour, he saw Regaud and Lacassagne, and was received with equal cordiality by Sabouraud.

Before leaving London, Doctor Stevens carefully examined the theory of Quinton concerning the therapeutic action of intramuscular injections of especially prepared sea-water, not only in affections of the skin, particularly psoriasis, but also in general debilitating conditions. He later analyzed and evaluated this method of treatment in three papers which appeared in 1909, 1912, and 1913.

The name of Dr. Rollin Stevens has been intimately and influentially identified with the radiological treatment of cancer ever since the inception of this procedure. His career has been actively associated more specifically with the changing phases of the roentgen therapy of this condition from the early day of its most superficial application. The available references to his literary contributions on the subject of cancer comprise at least sixteen papers

from 1904 to 1935. One of the most elaborate of these (1917) deals with the state of the blood in cancer under the action of roentgen therapy. Stevens therein discusses with ingenuity the question of the coincidence of reactionary lymphocytosis and roentgen therapy in the larger doses, submitting that the resulting general immunity, even though temporary, suggested by the presence of lymphocytosis may well be interpreted as one of the two-fold salutary effects of roentgen therapy in cancer.

Doctor Stevens was profoundly moved, as were all thinking radiologists, by the unfavorable reports of 1920 and 1921 regarding the incidence of aplastic anemia resulting from the cumulative effect of repeated exposure to radio-active emanations. Such untoward consequences were in direct line with his conviction, expressed years before, that occupational radiation, or therapeutic dosage of radiation, should be controlled by periodic blood examination as well as by continued inspection of the integument so exposed. He was a strong protagonist of the world-wide movement among radiologists toward the standardization of roentgen-ray generation and especially of methods of protection. This movement had its impetus, to which he added the force of his influence and wisdom, in the recommendations of the Roentgen-ray Protection Committee of the American Roentgen Ray Society, formulated in 1920 and finally adopted in 1922. These recommendations involved specifically the questions of apparatus standardization, filtration, accurate mensuration of dosage, periodic blood and basal metabolism investigation of operatives and periods of respite, all of which Stevens had previously emphasized.

Particularly in the matter of apparatus has he been interested. He first carefully watched each early advance in the development of radiotherapeutic devices, especially after the production of the hot-cathode tube of Coolidge, and has kept step with this evolution in connection with all installations under his charge. His was the second deep-therapy apparatus to be installed within the State of Michigan, the first having been an experimental model maintained by the General Electric Company at Battle Creek. His enthusiasm for the adoption of new ways and means in cancer therapy apparently knows no bounds. A 400-kilovolt generator was installed during the Spring of 1937 at his laboratory, but evidently the output potential of each new piece of apparatus he acquires can never quite keep pace with the peak E.M.F. of this astounding man!

Doctor Stevens' editorial in RADIOLOGY six or seven years ago under the title "Cancer Institutes" revealed, in the reading, a new light on his long-range vision concerning the cancer problem and the most potent means ultimately to solve it. One of them, he explained in this editorial, is the complete co-operation of trained experts chosen from various fields of scientific activity, notably surgery, pathology, radiology, biochemistry, and biophysics. Such complete and effective co-operation can be attained, he felt, only through the construction, equipment, and endowment of a Cancer Institute, based on lines of equivalent completeness. Stevens cited the various cities which then possessed institutes for the investigation of cancer, but deplored the fact that none of them had sufficient endowment. He expressed the opinion that, if and when an endowment proportionate to the purpose were available, it should be organized and controlled by private philanthropy rather than by the state or municipality, in order that the control of Institute activities by politics might be obviated.

To-day, Doctor Stevens has lived to see an organized movement to the end he visualized in 1931, thus far realized in the Congressional passage of Senate Bill No. 2067, which is a joint bill combining the generous appropriations called for by the Maverick Bill and the Bone-Magnuson Bill. This "will establish a National Cancer Institute and provide for the United States Public Health Service to aid and co-ordinate

research relating to cancer."[4] While this development does not completely conform to Stevens' conviction that such an endowment should proceed from private philanthropy, it is so epochal in its promise as to become one of the deepest satisfactions of his useful life.

During an installation of apparatus at his hospital laboratory in February, 1917, Doctor Stevens received accidentally the high-tension discharge from the terminals of a rotary converter. The shock rendered him unconscious and seriously affected his spine, from which injury he has never fully recovered. Those were "parlous times," it will be remembered, and shortly before this accident Stevens had made voluntary application for military service with either the Canadian forces or with the army of the United States at that time on the Mexican border—wherever roentgenologists were needed. When, in April, the United States entered the Great War and Base Hospital No. 2 was organized and recruited as a military unit, he was accepted and appointed as a Major of the Medical Corps to take charge of all bacteriological and x-ray work. When, however, the papers pertaining to his physical examination were reviewed at Washington, he was rejected. With business affairs arranged and uniforms made, his disappointment was bitter indeed. By the Summer of 1918 there was urgent demand for expert military roentgenologists for immediate service overseas. Stevens again volunteered and was promptly accepted, but his time in New York, the port of embarkation, was uselessly consumed in futile military drill and superfluous instruction. While there, he fell a victim to the severe influenza epidemic then prevalent and nearly succumbed. The Armistice was signed before his long convalescence was over.

Through all these years, except when interrupted by periods of illness or temporary absence from other causes, Doctor Stevens has faithfully fulfilled his duties of teaching, which began in 1904 as Lecturer on Dermatology at Ann Arbor. His formal teaching of roentgenology commenced in 1910 as Assistant Clinical Professor at the Detroit College of Medicine; he still gives there the courses of instruction in diseases of the skin instituted by him in 1925. In 1929, he was Extra-mural Lecturer in Post-graduate Medicine at the University of Michigan. His interest in research and research-teaching has been equally lively. He has been Secretary and also Director of the Radiological Research Institute. From the opinions expressed by those who have sat beneath his rostrum, or from the experience of those—interns, nurses, technicians—who have been in daily clinical contact with him, or from the joyous reaction of little children by the evening lamplight or in the open fields of summer, it is clear that Dr. Rollin Stevens is a teacher "to the manner born."

One of the notable features of the career of this altruistic physician is his loyalty and devotion to the welfare of the organized groups of medical men with which he is affiliated. He is an outstanding member of all four of the major American radiological associations—indeed, he has most worthily occupied the presidential chair of most of them. He became a member of the American Roentgen Ray Society but four years after the date of its organization; he is, therefore, one of its fourteen senior members, according to its present roster. He identified himself closely with the foundation of the Radiological Society of North America and was elected its President in 1924. He was President of the American Radium Society in 1933–34. He was active in the formation and organization of the American College of Radiology, of which he was a Chancellor from 1926 to 1929, its President in 1930–31, and again Chancellor from 1931 to 1936. Seeming never to become surfeited with the myriad cares and responsibilities of almost continual executive office he has thus filled from year to year, the records show

[4] *The Bulletin* of the Inter-Society Committee for Radiology. August, 1937.

that his management has been always effective, his judgment sound, and his decisions wise.

Doctor Stevens was one of a group of some fifteen representative American radiologists formed by himself in 1933 at the request of the American Medical Association to establish an American Board of Radiology for the purpose of standardizing the qualifications of specialists in this field. The labor involved in appointment to this Board is of a degree almost Herculean; Stevens' capacity for work, his tenacity of ideals and at the same time his tact and sense of fairness, may well be taken as the reasons for his recent reappointment to this Board for a term of six years.

Besides these activities, he is, of course, a Fellow of the American Medical Association and a member of his State and County Medical Societies; a Fellow, also, of the American College of Physicians. Other associations devoted to his two specialties of which he is a member are the Detroit Roentgen Ray and Radium Society, whereof he was President in 1926, and the Detroit Dermatological Society, over which he presided in 1927. The Canadian Radiological Society and the Chicago Roentgen Society have each made him an Honorary member.

In view of this brilliant record in the name of professional fellowship for the loftiest of ideals, one might think that Dr. Rollin Stevens has no added time, no reserve strength, for active and perhaps equivalent endeavor outside his chosen fields in Medicine. If such is his belief, let him consider other conspicuous facts in the history of this extraordinary man which, in addition, vividly exemplify his deep sense of personal civic duty, his solicitude for the social welfare of others, his unflagging interest in matters involving the public health. Evidence of all these qualities is revealed in the conception, foundation, and evolution of the Detroit "Ford Republic," a Home for delinquent boys named in honor of its generous benefactors, the late Mrs. E. L. Ford and her daughters. To this institution, which today produces results that are everywhere acknowledged, Doctor Stevens has given much time and great effort. To him its remarkable and renowned success is due.

Since 1907, Doctor Stevens has been particularly interested in the increasingly important question of social hygiene, probably by reasons of its relationship to his dermatological work. Many years ago he organized in Detroit the "Social Hygiene Society," composed originally of physicians, clergymen, and laymen but with the later wise ruling that only physicians should lecture under its auspices. The functions of this organization were notably effective, especially under his presidency, at a day when public opinion on this subject was lethargic and corporate action difficult to obtain. As Secretary of the Detroit Practitioners' Society and as Chairman of the Sanitation Committee of the Board of Commerce, his public spirit and medical acumen were later again revealed in a regulation to control promiscuous public expectoration and to rectify the system of garbage disposal.

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In spite of these contrastive interests, which exert a magnetic effect upon his enthusiastic and conscientious nature as well as a momentous drain upon his time and energy, Rollin Stevens is an earnest devotee to mental and physical relaxation. Wisely he seems to prefer the recreative advantages obtained from more gentle pastimes and less strenuous sport to the possible over-exertion of the links or of kindred exercise with but superficial purpose. Yet, because of his love for children and theirs for him, he is ever ready to join with spirit in their festivities out-of-doors or in—whether it be an Indian dance around a picnic bonfire or reading aloud from a storybook. It is the hemoglobin of human love that brightly colors his blood and dispels all physical effect of the passing years, as they seem silently to arrive and to depart in the diaphanous garb of unreality.

Doctor Stevens' real respite from toil, however, is his wholesome absorption in his several avocations, chief of which are mycology and conchology. He makes periodic field excursions in search of mushrooms and expeditions after rare molluscs; sources of never-ending delight that only the true collector can know. Not only was he for years the President of the Detroit Mycological Society, but he has a national reputation as a mycologist. One of the several varieties of mushroom he has discovered has been officially named for him—*Helvella stevensii*. In 1934, as a note of warning to unsophisticated collectors, he (with Mr. Wendell Holmes) described in the periodical *Hygeia* the natural characteristics of a peculiarly poisonous variety, the *Amanita*.

The buoyancy of Stevens' philosophy of life is the probable reason why even those who see him infrequently observe so little physical change in him; even less is noted by his closer friends. "To-day, at seventy," writes one of his intimate associates,[5] "he hardly seems to have changed since the time I first met him fourteen years ago. His posture, his features, his reactions have altered him but very little. . . . He works as hard and as many hours as ever."

The copious career of Rollin Stevens, observed by his friends as from their task they turn their eyes his way—perhaps for the reassurance of high example—reveals how industriously, how studiously, how productively, and withal how joyously, the age of seventy years may be approached and reached!

[5] Dr. Hans A. Jarre, *Personal Communication*.

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THE RÔLE OF RADIOLOGY IN MEDICINE[1]

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THE International Radiological Congresses have made it a rule to place on their programs, in addition to the scientific questions, radiological-organization problems of general interest for medicine as a whole. The present Congress has placed on its program for discussion that most central of all radiological-organization problems: *the integration of radiology into medicine as a whole.*

The President of this congress, Dr. Arthur Christie, and Dr. William Mayo, America's world-renowned surgeon, ruler of one of the metropolises in the realm of medicine, have displayed for us their broad view of one side of the problem: *the unity of medicine.* To me has been given the honorable task of opening the discussion of the problem's other side: *the rôle of radiology as a member of the unity of medicine.*

For the one who can remember the birth of radiology, the story of the development of this science is a marvelous one. The new light became visible like a dazzling meteor in the evening of the nineteenth century. It surrounded the morning of our own century with the rosy light of hope and promise. Like a glittering sun it shines resplendent on the working day of the twentieth century, revealing new fairways and fresh horizons in nearly every land in the world of science.

In medicine, radiology has played the rôle of a *pioneer* and a *creator* in the spheres of diagnostics and of therapy.

Its revolutionizing work in the *domain of diagnostics* is that it has extended the physician's field of vision to include the interior of the living man. Roentgen diagnostic methods have increased diagnostic skill in almost every branch of the medical science, and in this way have contributed in a high degree to the reliability of our judgment of the indications of treatment and have thereby improved the results of treatment. I will merely remind my hearers that roentgen diagnostics have contributed most essentially to the magnificent progress made during the present century in the provinces of abdominal, thoracic, and cerebral surgery, and in orthopedics. As regards internal medicine, too, roentgen diagnostics have become an indispensable guiding star.

Also radiotherapy, that is, Finsen-, Roentgen-, and Curie-therapy, has created an epoch in the history of medicine. By its destructive action on malignant tumors and dermatic fungi, by its power of hastening or causing a healing process in inflammatory conditions of various kinds, and by its readjustive action on certain disturbances in the functions of the endocrine glands and the hematopoietic organs, radiotherapy has become an indispensable weapon in the service of medicine.

But how is it that radiology has come to play such a rôle that one is entitled to say it has set its seal most decisively on the medical science of the present century? And how, in the future, will radiology be able to continue to play this important part?

All development in living Nature has arisen by means of progressive subdivision of labor and by the differentiation of special organs for special tasks, to which must be added, co-operation between these organs.

New tasks demand the differentiation of new working organs, and awaken to life new forms of co-operation. This law of the differentiation of special organs, for tasks which are of importance for the entire organism, holds good also in the development of medicine, and, as a matter of fact, has given rise to the differentiation of radiology into a special discipline in medicine.

[1] Opening lecture at the Fifth International Congress of Radiology in Chicago, Sept. 13–17, 1937.

This differentiation took place simultaneously with the entrance of radiology into the field of medicine. It was brought about by the necessity of controlling certain parts of radiophysics for certain medical purposes, and of possessing technics, based on this control, for medical examinations or treatments. These examinations and treatments demanded, in their turn, special training, special equipment, and special premises and, finally, special roentgen departments at our hospitals.

Consequently, during the first few years of this century, radiology played the part of a physical auxiliary science in the service of medicine. At the hospitals, radiologists had the rôle of being physical and technical assistants to the head doctors at the clinics.

The differentiation of radiology into a special branch of practical medicine, equal in rank to the other disciplines of medical science, was brought about by the development of radiology—through the scientific elaboration of the results of its work in the field of medicine—into a medical science which demanded the entire ability of its practitioners.

The next step was that the importance of radiological science in the general training of medical men increased so much that a chair had to be found for it in the medical faculties.

The differentiation of radiology into an independent medical discipline has proceeded on parallel lines, but not always simultaneously, within the organizations which constitute medicine's general staff —the medical faculties—and its army in the field — the institutions where medicine is practised.

The development of the part played by radiology at the hospitals and in the faculties has varied much in different countries, and even in different parts of the same country. This is often the result of external causes, especially those originating in a want of financial resources during the critical times in which we now live. Principally, however, the struggle for the recognition of radiology as an independent member of the unity of medicine has led to victory.

Many actual organization problems exist in every country, however, when it becomes a question of such a practical embodiment of the radiological institutions in the hospitals of to-day as will enable the hospitals to fully utilize the conquests made by radiological science. Nowadays, the actual organization-problems are not caused, in most places, by the external differentiation of radiology. It is necessary, first and foremost, to find a practical organization, corresponding to the internal differentiation which, during the last few decades, has taken place within radiology in consequence of the subdivision of labor and the specializing necessitated by the two main tasks of medical radiology: roentgen diagnostics and radiotherapy.

This internal differentiation has, on the whole, followed the same path of development as that taken by the external differentiation of radiology in relation to the other disciplines in medical science. The specializing of the technics and the growth of the clientele gave the first impulse to the division of radiology into two branches. The innermost cause of this cleavage of medical radiology is to be looked for, however, in an essential difference which exists in the scientific basis of each branch of radiology.

Although the roentgen rays are the common source of roentgen diagnostics and roentgen therapy, still, in regard to their scientific character and their practical employment, they are as widely different from each other as are histology and heliotherapy. The one employs the optical properties of light in the service of medicine; the other makes use of its biological effects.

Roentgen diagnostics is a branch of *anatomy. It is the science of man's normal and pathological structure as it appears in the roentgen picture. Radiotherapy*, on the other hand, *is a branch of physiology. It is the science of the action of the different rays on the organism in conditions of health and sickness.*

Roentgen diagnostics and radiotherapy demand different scientific training, and the investigation of each belongs to different spheres of medicine. The conditions necessary for their practical utilization are also very different.

Many co-operating, external circumstances, too, have contributed during the last two decades toward the rise of separate institutions for roentgen diagnostics and radiotherapy. But no factor has been more active in this matter than the conquests made by Roentgen- and Curie-therapy in the domain of malignant tumors. Radiotherapy's task of treating about two-thirds of cancer patients, alone or in co-operation with surgery, has, even from a mere practical point of view, made it impossible for one and the same man to satisfactorily direct both the roentgen diagnostic work and the radiotherapy of a large hospital, if he is not a genius.

At most places, this cleavage process in radiology is still in a latent stage. But at this very moment, there are numerous radiologists who are sinking under the impossible task of endeavoring to maintain roentgen diagnostics and radiotherapy on a level with the development of the sciences. At the same time, at most hospitals, financial, technical, and staffing reasons make it impossible to divide the radiological work between altogether different institutions.

It is only where radiology has most vigorously developed that the diagnostic and therapeutic laboratories of the radiological hospital departments have been able to develop into separate institutions. At most places, however, the two branches still remain under the direction of one and the same radiologist. At a number of large hospitals which have become centers for the treatment of cancer, independent radiotherapeutic clinics have been established in addition to the radiological services. It is only at a few places, however, that the chiefs of the latter have been relieved from therapeutic work, and allowed to devote themselves entirely to roentgen diagnostics.

A complete divorce between roentgen diagnostics and radiotherapy confers such great advantages, both for research work and instruction, as well as for the utilization of radiology in practical medicine, that I consider one of radiology's highest hopes to be the division, as soon as possible, of the radiological work, at university and other large hospitals, in order to embrace separate and independent roentgen diagnostic and radiotherapeutic departments.

The divorce between roentgen diagnostics and radiotherapy at the large hospitals, together with the increasingly extended demands on radiology made by every branch of medicine, makes actual the question of a further differentiation of each of the two main branches of radiology.

A differentiation within roentgen diagnostics has taken place in consideration of the demand for special knowledge of certain branches of roentgen anatomy, and for special technical skill in roentgen examination of various organ systems.

The central roentgen departments which are overburdened with both therapy and diagnostics, have not infrequently been faced by special tasks for which they have been wanting in both time and staffing. The result, at many places, has been a disruptive transference of roentgen diagnostics to roentgen diagnostic laboratories at the different clinics. Such a transference has been necessary also where the various departments of a hospital have stood apart, and without any convenient interior means of communication with each other.

A concentration of the various branches of roentgen diagnostics to a central roentgen diagnostic institute is, however, a desirability of the utmost importance. If a roentgen diagnostician is relieved entirely of the tasks of therapy, he will then be well able to control and direct the work in all the branches of roentgen anatomy by himself, just as the professor in histology is able to control the whole of his province and its immediate surroundings.

A central institute of diagnostics offers great economic advantages, both in regard to the current working and also in respect to the maintenance of the equipment at an

up-to-date level. It provides all the departments of the hospital with opportunities of keeping themselves *à jour* with the development of roentgen technics and roentgen diagnostics in every sphere of medicine. It offers the physicians, and the other staff members of the roentgen institute, great and all-round experience. Above all, a central roentgen institute constitutes a necessary condition for conveying scientific and all-round instruction in roentgen diagnostics.

A centralization of roentgen diagnostics at a hospital is possible only under certain conditions, however. For instance, there must exist good indoor communication from all the hospital departments to the roentgen diagnostic institute, and the cooperation of the latter with those departments which are to be served by it must be organized in such a way that it will act as if every hospital department was provided with its own roentgen diagnostic section. The director of the roentgen diagnostic department must have at his side a staff of assistants who have been specially trained in the various branches of this science and who have at their disposal the necessary special equipment. Our experience in Sweden shows that there should be one assistant roentgen doctor for every 100 to 150 beds at a general hospital with both clinical and polyclinic departments.

The size of the central institute must be so far restricted, however, that it will not have to work for more than about a thousand beds and the corresponding out-patient departments. If the hospitals are larger, then a number of clinics should be grouped around central roentgen diagnostic institutes.

But even if there be carried out as complete a centralization as possible of the roentgen diagnostic institutes, still there must be smaller roentgen laboratories at each clinic where there can be carried out such roentgen examinations—fluoroscopic, especially—as have to be made in immediate connection with other examinations or with treatments.

Within radiotherapy an interior differentiation has occurred, in respect to the radiotherapeutist's need of knowledge of the special pathology and clinic of the diseases which he has to treat. As long as the radiologist is not a master of the clinic of the diseases he treats, he must remain a technical assistant of the clinician. But all experience has shown, however, that one and the same physician must possess both technical and clinical skill if the resources of radiotherapy are to be fully utilized and have a possibility of development.

Differentiation in radiotherapy has taken place, either by hospital departments for radiotherapy having been created in connection with certain clinics—surgical, gynecologic, and dermatologic, especially—or else by special sections for the treatment of certain organ systems having been added to general radiotherapeutic clinics. The most usual reason for the creation of special radiotherapeutic departments at hospitals has been the greatly increased demand for radiotherapy in cancer. These radiotherapeutic clinics have led to a considerable development of radiological cancer therapy. By their side there have arisen research institutes for radiophysics, radiobiology, and radiopathology which are of inestimable value for the further development of radiotherapy.

If radiotherapy is to fully utilize the rich possibilities it possesses also within the sphere of internal medicine, it should seem necessary to open, as soon as possible, radiotherapeutic wards at the clinics for internal medicine, or else at the general radiotherapeutic clinics, for the treatment of such diseases where radiotherapy is the main factor in the treatment, but which, in other respects, fall within the sphere of internal medicine.

We know that medical research is the basis of practical medical science. If a country is to utilize the progress made by radiology, it is, first and foremost, necessary to create a staff of teachers of radiology and institutions for research and instruction in radiology at the universities.

But this will not be enough. If the progress made by radiology is to benefit

the whole country, then, in addition, the radiological institutes of the general hospitals must be so organized that they will be able to keep pace with the rapid development of radiology.

To find recruits so as to be able to create a body of fully trained roentgen diagnosticians and radiotherapeutists, the leading physicians at the radiological departments of the hospitals must be offered such terms of engagement that they will be able to devote themselves entirely to radiology. They must also be provided with sufficient assistance to prevent their being altogether absorbed by the practical work of their department. They themselves must have rich opportunities for studying the further development of their science. Every leading radiologist who wishes to keep up with the times must, in addition to carrying on his work as a doctor, also play the part of a constructor and organizer, so as to be able to regenerate and rejuvenate his department.

Each general hospital of any great size, then, should be so equipped that, for its town and its district, it can play the part of an annex to university institutions. Without such a parallel organization in the hospitals of a country, the medical schools may be compared to broadcasting senders which have no receivers.

With us, in Sweden, it is the task of the State to provide doctors with their general training. The duty of providing special training and the post-graduate instruction falls, above all, on the authorities who have charge of the practical care of the sick. The radiological departments of the large hospitals must, at one and the same time, be organs for the care of the sick, and post-graduate schools for radiologists. This is as much to the advantage of the patients as to that of the instruction.

Radiology has become more and more specialized and attached by ever firmer bands to the hospitals. Only as a limb of a hospital organization, and in co-operation with the other disciplines, can it be developed to perfection. The radiological departments of the hospitals, then, will remain the headquarters of radiological work. The development of the technics and the science of radiology will, too, in the future, demand deeper and wider knowledge on the part of the specialists in the sphere of radiology.

On the other hand, the radiological sciences are gaining ever increasing clarity; their technics are becoming simplified, and the instruction is developing in such a way that certain parts of radiology will be a possession of the general practitioner. Nay, the time will probably come when a roentgen outfit will be as necessary a part of a doctor's equipment as a microscope. In the same degree, the demand for radiological specialists and for further research into, and instruction in, radiology will increase.

In Sweden, the organization of the institutions for the training of radiologists, and of the radiological departments at the hospitals, has, on the whole, been carried out in agreement with the principles laid down above.

Regular instruction in radiology is given at the three medical faculties in Sweden. At the Caroline Institute, in Stockholm, the instruction in radiology has, since 1936, been divided between two ordinary professorships; the one, in roentgen diagnostics, and the other in radiotherapy. At Upsala, there is a professorship in the entire subject of medical radiology. At Lund, the medical faculty has applied to the Government to change the lectureship in radiology into one in roentgen diagnostics and, in addition, to found a professorship in radiotherapy.

At all the medical faculties in Sweden, there is given a course of lectures (six weeks), obligatory for medical students, at the commencement of their work at the clinics. Beside this, there is a course of instruction, with practical training (two months), at the close of the medical studies, attendance here being voluntary.

Special training in radiology can be had by serving as assistant doctor in radiological departments for a period of from three to five years, after having previously

acted as assistant doctor for, as a rule, two years at surgical and medical clinics. Practical training in radiology, for such doctors as do not intend to devote themselves to radiology as a specialty, is gained by working as an assistant for from six to twelve months at radiological departments.

Complete radiotherapeutic clinics exist in Sweden, a country of about six million inhabitants, at three hospitals, namely, at the University Hospitals at Stockholm and Lund, and at a large public general hospital in Gothenburg. At these three hospitals, the departments for radiotherapy and for roentgen diagnostics are quite separate from each other, each being in the independent charge of a radiologist.

At the new public, general hospital in Stockholm, now in course of erection, the same division of the radiological work will be carried out. At 41 of the country's other hospitals, there exist undivided radiological departments. Hitherto, the rule has been followed that, when a hospital has grown so large that separate medical and surgical departments have been created, there also has been established an independent radiological department.

At the smaller hospitals, there are only diagnostical roentgen laboratories which are in the charge of doctors who have received a short special training in roentgen diagnosis. Practically speaking, all radiotherapy is referred to and carried out at the hospitals which have independent radiological departments in the charge of radiologists specially trained in radiotherapy. Radiotherapy in cancer is not confined to special cancer hospitals but is practised at the radiotherapeutic clinics or the radiological departments of the hospitals.

The radiologists stationed at the hospitals are at liberty to carry private radiological practice, in addition to their official work, at their departments, and the head physicians at the radiotherapeutic clinics have rooms for private patients at the clinics. As a rule, consequently, a radiologist carries on all his work at his department at the hospital.

By what I have now said, I have endeavored to describe the rôle played by radiology in relationship to other branches of the medical unity, and the ways by which, I consider, this science is to move onward as the representative of light in the domain of medicine. But whatever the rôle played by the different disciplines of medical science in respect to each other, and to the other organs of the community, all those who exercise the work of a physician have, first and foremost, to be the servants of their science and of that community. The strong band uniting the various branches of medicine into a unity is the common task of serving suffering humanity; of attempting to prevent, or to cure, disease.

The whole of our training and all our daily work should be devoted to the carrying out of that common duty, and thereby rendering mutual help to all, and no one, I think, plays that rôle more often than does the radiologist, acting as a servant of his comrades in the unity of medicine.

Therefore it is that the radiologist, if he pursue his call rightly, constitutes a link between the representatives of practical medicine. This rôle of the radiologist finds eloquent expression at the general hospital of to-day by the fact that the radiological institute constitutes the daily meeting place of the heads and the staffs of the various clinics.

The International Congresses of Radiology, too, have proved an important link between nations. I would like to remind my hearers that the First International Congress of Radiology in London, in July, 1925, was the first international scientific congress that assembled after the Great War. Since that date, four congresses have brought together multitudes of radiologists from every country of the globe to co-operate in the work of science.

To conclude, it is my pleasant task to express warm homage and sincere thanks to the radiologists of the United States of America for the important part they have played as engineering technicists and scientific investigators in the development

of radiology. I need but mention the names of Caldwell, Francis H. Williams, Janeway, Lewis Gregory Cole, Preston Hickey, George Pfahler, James Ewing, and George Holmes, all of whom have contributed to lay the foundations of the science of radiology.

I also beg to thank and to congratulate the President, the Secretary General, and the National Committee of the Fifth International Congress of Radiology for the brilliant part this Congress plays in the line of these international gatherings, both by its scientific program and by its calling us together in such a delightful way to this feast of comrades.

I feel convinced that this Congress will bear rich fruit in the field of radiological science, and that history will bear witness that it has most devotedly carried out its task of serving a suffering humanity.

CONTRIBUTION TO THE PATHOLOGY AND CLINICAL PICTURE OF RETICULUM-CELL SARCOMA[1]

By LARS EDLING, M.D., *Lund, Sweden*
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THE affections of the reticulo-endothelial system have long been the object of most lively interest on the part of the pathologists. In recent years, the malignant tumors arising from the reticulo-endothelial tissues, in particular, have attracted the attention also of the radiologists, and it therefore seems to me a suitable subject to bring before this Congress, especially as there are several questions in this connection that are in need of further discussion.

PATHOLOGY

Already, in 1914, Ewing had discerned a species of tumors emanating from the reticulum cells of the lymphatic tissue, and in his text-book he definitely speaks of *reticulum-cell sarcoma* as different from the *lymphocytoma*.

In 1930, Roulet, of Berlin, described in detail, under the name of *retotheliosarcoma*, a group of tumors arising from the lymphatic tissue in lymph nodes, the epipharynx, the tonsils, and other parts of the upper air passages—growths which are doubtless identical with the above-named reticulum-cell sarcomas of Ewing, but which other earlier investigators generally had not noted as different from other lymphogenic tumors and had classed, therefore, under the general heading of lymphosarcoma. Now, Roulet showed that they do not derive from lymphatic cells, but from the reticulum cells of the lymphatic tissue. On account of their varying histologic characters, Roulet suggested the division of them into three groups, as follows:

(1) The *immature*, or *undifferentiated*, type. The tumor is built up of a uniform syncytium of large, pale, round, and polygonal cells, anastomosing with each other through abundant strands of cytoplasm. The cells have a large, bulb-shaped nucleus with finely divided chromatin, a distinct nucleolus, and a sparse cytoplasm, often containing numerous droplets of fat. This comparatively rare form is considered by Roulet as the *primary type of retotheliosarcoma*.

(2) *Mature forms*, characterized by the tendency of the tumor cells to develop fine fibrils which arise within the plasma, but with tumors of a higher degree of maturity are seen to enlace the cells of the syncytium as a wide-branching network. In the early stages this fibrillar network becomes apparent only on staining with silver, but with greater differentiation it can in part assume a collagenic character. In sections, the youngest portions within the syncytium—the centers of proliferation or "*Brutstätten*"—appear as areas more or less entirely free from fibrils.

(3) *Associated or combined forms* are those in which the blastomatous process in the reticulo-endothelium is combined with pathologic proliferation also of other cellular elements, such as a leukemia or lymphogranulomatosis. Thus, Roulet establishes a connection with the investigations of Oberling, in which the latter author, makes a distinction between two main groups of *reticuloses* and *reticulo-endothelioses;* namely, pure and associated. The latter are combined with proliferation of hematopoietic cell types leading to the simultaneous development of leukemia, lymphogranulomatosis, aleukemic lymphadenosis, or pernicious anemia. Oberling even describes combinations of reticulosis and reticulosarcoma, and characterizes Ewing's sarcoma as a form of reticulosarcoma localized to the bone marrow.

Next to Roulet, important contributions to the histopathology of these tumors have been rendered by Ahlström, of Lund. In conformity with Ewing, he has preferred

[1] Presented before the Fifth International Congress of Radiology, Chicago, Sept. 13–17, 1937.

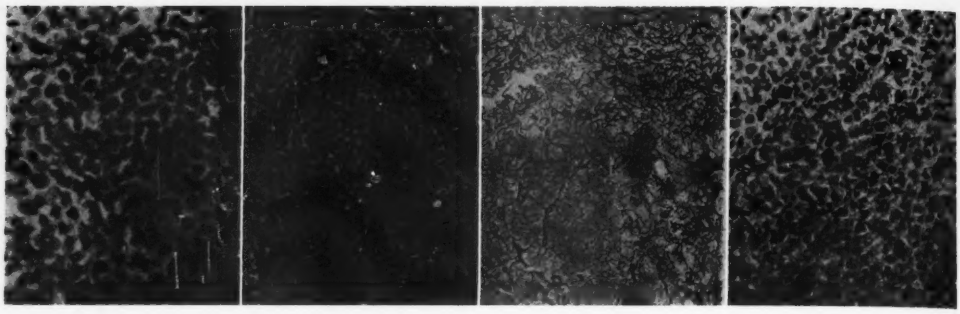


Fig. 1. Fig. 2. Fig. 3. Fig. 4.

Fig. 1. Case 1. Immature type of RCS. Silver staining (Perdrau). Only very solitary fibrils are seen in the syncytium.
Fig. 2. Case 6. Cell syncytium, fibrillogenic type of RCS. Hematoxylin (v. Gieson).
Fig. 3. Case 4. Fibrillogenic type of RCS. Fibrillar network with *Brutstätten*. Silver staining (Perdrau).
Fig. 4. Case 10. Polymorphocellular type of RCS, with giant cells. Hematoxylin (v. Gieson).

the name of *reticulum-cell sarcoma*, because the reticulum cells are not cells overlying a preformed reticulum, but themselves form a cytoplasmic reticulum. In Sweden, therefore, we have generally adopted that appellation (RCS).

Ahlström links up with the works both of Roulet and of Oberling, and he points out that the varying morphology of the cells in RCS can be referred to the inherent possibilities for differentiation of their mother tissue, the normal reticulum cells. The primary type also of these is a simple syncytium, the cells of which have evolved from the primordial mesenchyma, and which therefore are capable of developing in different directions. As supporting tissue for the lymphatic elements they have a tendency to develop a fibrillar reticulum; as active mesenchyma cells they are able to organize themselves as free macrophages, or eventually pass into the blood as monocytes; under pathologic conditions they may change into giant-cells.

Ahlström believes that it is not possible to draw a sharp histologic line between the different forms of RCS, but that we must confine ourselves to a classification having in view the *predominant* morphologic characters of the cells. On this basis he sets up, in addition to Roulet's immature and fibrillogenic types, a third group, *viz., the polymorphocellular type*, characterized by extremely varying forms of cells, round, polygonal or highly irregular, often connected with each other by protoplasmic offshoots, so as to form continuous synplasmas. Often the cells are developed into phagocytes. Another typical feature is the occurrence of numerous giant-cells with lobed or fragmented nuclei. Differentiation of fibrils susceptible to silver staining occurs, but not as a predominant character of the picture.

The interpretations of Ahlström have later (1936) been confirmed by Sjövall, of Lund, who calls attention to the resemblance of the proliferation centers of the growing tumor tissue to the secondary follicles of lymph glands (the reaction centers of Hellman), and points out that the diagnosis of RCS must be ascertained by the appearance of such centers surrounded by an argentophilous fibrillary network, and further through the demonstration of fatty substance in the syncytium cells, both necessary features in the picture of RCS.

Of other works from the last few years, in which RCS is dealt with from the pathological point of view, I will in this connection mention only De Oliveira's compilation of

20 thoroughly studied postmortem cases from Roessle's institute. He concurs in the main with Roulet and Ahlström, but has tried to carry the classification still further, and sets up six different groups, though without strictly drawn limits. Of these groups, his No. 6 is especially noteworthy, because it represents a very uncommon differentiation of the reticulum cells, namely, to lymphocytic elements and plasma cells. This is an interesting confirmation of the belief already expressed by Oberling, that the reticulum cells ought to possess just such a prospective tendency to differentiation also in a hematopoietic direction.

My own material consists of 18 cases of RCS, 17 of which are pure, and one associated (namely, with lymphatic leukemia). To these, I have in the following observations added two cases of generalized reticulosis which present certain points of interest. All cases were verified by biopsy, six of them, in addition, by examination postmortem. Cases 1 and 2 arose from the nasal and maxillary cavities, respectively; Cases 3–6 were epipharynx tumors; Cases 7–12 tumors of the tonsils; Case 13 arose from the hypopharynx; Cases 14–18 may be considered as primary lymphoglandular tumors.

Histologically, Case 1 must probably be classed as belonging to the immature type, or at least it is closely related to it. The majority (nine cases) belong to the fibrillogenic and three to the polymorphocellular group. In three cases material for an exact classification is lacking.

For details of the structure, I wish here to refer to the following reproductions of my photomicrographs which I think will demonstrate, better than any description, the characteristic features of the respective types of tumor.

The diagnosis of RCS must, of course, be based on microscopy. According to Baumann-Schenker, it should be relatively easy to distinguish an RCS from other sarcomas occurring in the upper air passages, such as lymphocytoma,[2] round-cell sarcoma, etc. Therefore, I will not dwell on this side of the question, but will confine myself to some words about the relation of RCS to a couple of other tumor groups, where discussion seems to be called for.

This is, first of all, in regard to the so-called *lympho-epithelioma*, described first by Schminke and Regaud. According to Schminke, they ought to be considered as branchiogenous tumors, built up of an *epithelial* syncytium, the cells of which are reticularly arranged and are more or less interspersed with lymphocytes which are considered to form an integrant part of the tumor's structure and to vegetate in symbiosis with the epithelium. In the periphery there is an abundant fibrillar network, which, however, does not penetrate into the actual neoplastic syncytium. Schminke calls attention to the fact that the resemblance to a sarcoma is great in the early stages. By Regaud and his pupils these tumors are considered as belonging to the carcinomas; also Roulet mentions them as a special type of tumor, under the name of *lymphocarcinomas*.

In Lund we have, since the appearance of Schminke's publication, been looking eagerly forward to a chance of diagnosing a lympho-epithelioma, but so far we have not met with any case of that kind. On the other hand, we have observed a considerable number of RCS, of which my material from the radiological clinic forms a part. We have begun, therefore, to suspect that many of the tumor cases described as lympho-epitheliomas have in reality been RCS. We base that belief on the following reasons:

To begin with the *histological* view of the question, Schminke and Regaud have, as before mentioned, adopted the theory of Jolly and Mollier, that the lining epithelium of epipharynx, the tonsils, and the basal parts of the tongue has been modified by symbiosis with the lymphocytes and, therefore, is to be regarded as a special organ, the *lympho-epithelium*, which, according to

[2] I have adopted the term proposed by Ewing because it seems to me to define the nature of this growth more accurately than the name of lymphosarcoma, commonly used.

Jovin, forms the origin of lympho-epithelioma. Ewing, for his part, seems to accept this standpoint to a certain extent, and admits that the lining epithelium is peculiar in structure, whence it would seem reasonable that the tumors arising from it should have special qualities. On the other hand, he emphasizes the great difficulties of discerning lympho-epithelioma from the tumors arising from transitional epithelium.

For a correct interpretation of the tumors in question, it seems to me necessary to consider the general function of lymphatic tissue and its relations to the epithelium. For instance, the lining tonsillar epithelium of the new-born, according to Hellman, whose works on lymphatic tissue enjoy general esteem, holds but solitary lymphocytes, but by the age of one and one-half years they have become very abundant and remain so until puberty, after which time they soon vanish more or less completely, in parallel with the proceeding involution of the tonsil. Hellman holds forth that this interspersion with lymphocytes must be regarded as a link in the chain of protective actions against bacteria performed by the lymphatic tissue everywhere in the body and that the intimate symbiosis between lymphocytes and epithelium presumed by Jolly and others is only hypothetic.

Strong supportive evidence for this opinion is supplied by the conditions in the intestinal wall. As well in the intestinal epithelium as in the submucosa there are, under ordinary circumstances, lymphocytes in great quantities, but these will disappear when the fecal contents of the bowel are freed from bacteria. This is shown by Glimstedt in guinea-pigs bred with completely sterile food: the lymphocytes are then entirely lacking in the intestinal wall. As far as I can see, there exist no reasons why this cell infiltration should have another purpose when occurring in tumors arising from lymphatic regions.

The histologic structures of an RCS and a lympho-epithelioma can without any doubt resemble each other very closely. It ought probably to be extremely difficult, microscopically, to distinguish whether a cell syncytium, growing in such a topographical environment, is of an epithelial or a sarcomatous kind. At least this difficulty will remain until the differential diagnosis has been supported by a difference in the type of cellular nuclei or by the tendency of forming an intraplasmatic fibrillar network. (As to the differential diagnosis against transitional cell carcinoma, see later in this paper.) At all events, the many morphologic varieties characterizing these tumor species must be considered.

I have tried to show why I think the theory of a specific lympho-epithelium cannot very well be maintained. I have examined my material with regard to the presence of lymphocytes, and have found that in three cases they are present in very large quantities in all parts of the tumors, in seven cases they are numerous about the vessels and in peripheral streaks of connective tissue, but comparatively sparse in the cell syncytium proper. In six other cases the interspersion is very scant, except in the peripheral connective tissue. To the last group belongs my Case 1, characterized above as probably immature. In this respect there will thus be found great variations in RCS.

As an argument for the specificity of lympho-epithelioma, some authors (Regaud, Hoffmann, v. Zalka) lay stress upon the fact that lymphocytes form an integrant part also of the metastases. For my part, I should think that their rôle in the metastases ought to be the same as I have above maintained regarding the primary tumors. At present, I cannot tell to what extent lymphocytic elements may enter into the composition of metastases from RCS (to alymphatic organs), but I presume that this will depend on the presence of infection. In my Cases 14, 16, and 18, in which such metastases were examined histologically after death, we found no lymphocytes worth mentioning.

Further, the epithelial origin of lympho-epitheliomas has been argued on account of their occurrence also in the thymus, which is considered as an essentially epi-

thelial organ. Now, the thymus is, from a biological standpoint, quite different from the tonsils and the lymph glands, and its "lymphatic" tissue has another structure than these organs, so far as it lacks reaction centers. Probably, its function also is different. As to the histologic nature of the growths of the thymus, the views of different authors stand in marked opposition to one another. Perhaps the existence of lympho-epitheliomas of the thymus, therefore, ought to be subject to further research.

However. the most important difference between the histologic pictures of lympho-epithelioma and RCS is said to be the entire absence of intraplasmatic fibrils in the syncytium of the former (v. Zalka, Jovin, and others). As to this, we must remember that also the immature forms of RCS, such as described by Roulet, Ahlström, and De Oliveira and as to a certain extent represented also by my Case 1, more or less completely lack fibrillar differentiation. In a certain number of cases, therefore, it is doubtful whether the lympho-epitheliomas are in reality identical with immature forms of RCS. Considering the diagnostic difficulties against transitional cell carcinoma (Ewing), one might justly suppose that in other cases this tumor species has been falsely diagnosed as lympho-epithelioma.

Clinically, the RCS in most respects seems to answer very well the descriptions of lympho-epithelioma. Both the localization and the general manner of growth of the primary tumor, as well as the pictures published (for instance, those reproduced by Berven in his work on the tonsillar tumors), show a strong resemblance to the characters of our RCS. The early formation of metastases with their markedly mesodermal character (see below), and the very pronounced tendency to generalization, are common for both. Hoffmann admits that the differential diagnosis of lympho-epithelioma, clinically, is uncommonly difficult. On the other hand, some authors (Ewing, Jovin, personal statements) have maintained that lympho-epithelioma as a rule grows more slowly and often becomes first manifest a long time after the regional metastases have appeared. These tumors may remain small and well defined for months, whereas the RCS tumors are said to have a more pronounced tendency to infiltration. Such small tumors may be completely removed and show an epithelial structure. For my part, I must remark that we have never observed any such cases in our material as could deserve the name of lympho-epithelioma, but there have been some few that most assuredly have been transitional-cell carcinoma.

Finally, the two tumor species resemble each other also in their very noticeable, intense radiosensitivity; in which respect the so-called lympho-epitheliomas differ also from the ordinary carcinomas of the pavement-epithelium type.

In the course of my investigations, I have received some support for my views also from the pathologists and clinicians of the Radiumhemmet in Stockholm. The earliest cases of lympho-epithelioma in the material of that institution were diagnosed histologically by Albertini, of Zürich; and in the beginning the guiding-lines for the diagnosis thus established were followed at the Radiumhemmet. I here reproduce (Fig. 6) a photomicrograph of such a case which is included in Berven's material and has been placed at my disposal by the courtesy of the pathologist, Dr. Reuterwall. As the works of Roulet and Ahlström became known, however, both this and other cases of lympho-epithelioma were, on subsequent scrutiny, transferred by Reuterwall to the group of RCS. As a matter of fact, the illustration reproduced shows on many points a great resemblance to the following photomicrograph (Fig. 7) representing a section from my Case 13.

Another group of tumors in the upper air passages that can easily be confused with RCS are the *transitional-cell carcinomas*, first described by Quick and Cutler. With regard to the diagnosis of these tumors, Schinz and Baumann-Schenker, in their article published in 1936, have satisfactorily made clear both their pathogene-

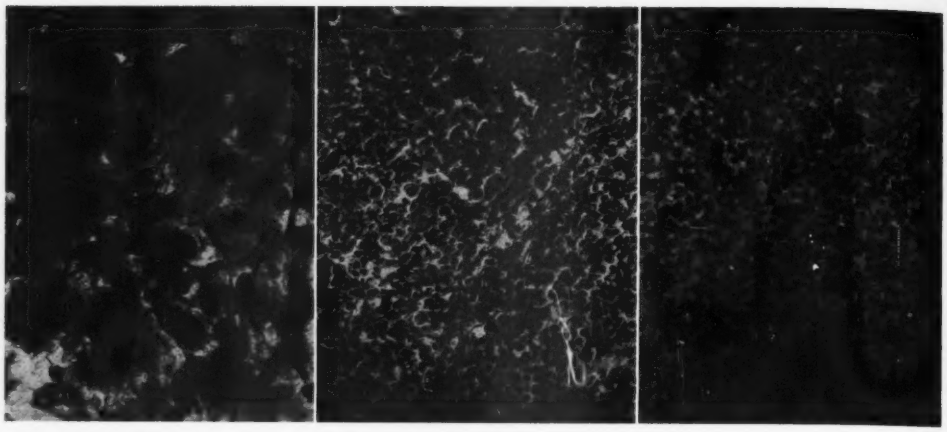


Fig. 5. Fig. 6. Fig. 7.

Fig. 5. Case 10. Polymorphocellular type of RCS. Silver staining (Perdrau).
Fig. 6. Case classed as lympho-epithelioma at the Radiumhemmet, but afterward transferred into the group of RCS.
Fig. 7. Case 13. RCS of fibrillogenic type. Note close resemblance to Figure 6.

sis and their manner of growth. Ewing, however, seems to be the one who has devoted most labor to this research. As before mentioned, he especially states the difficulties in distinguishing them from lympho-epithelioma. According to our experience in Lund, several tumors of this kind may also present, in different parts, a great resemblance to RCS, the arrangement of their cell tissue often being confused or even reminding one of a syncytium. However, in the majority of cases there will probably, at least in some places, be found the alveolar disposition of the cells generally characterizing a carcinoma. Further, their nuclei have another aspect and lastly, these cancers lack the fibrillary differentiation characteristic to most RCS.

Clinically, one finds many characters strongly reminding one of an RCS. The outer shape of the primary tumor is, though, usually not so voluminous as in the latter, but more flattened, and very unlike that of the pavement-epithelium cancer. The early metastases which sometimes are manifest even months before there is any demonstrable sign of primary tumor; the rather marked tendency to generalization, and the considerable radiosensitivity—all these are characters that may also be found in RCS.

In Lund, we have, during the period 1930–1936, had 12 cases of transitional-cell carcinoma, or, as we used to call it in Sweden, undifferentiated cancer, of the nasal cavity, the epipharynx, and the fauces. Only one of them has, in an early stage of its course, been transferred to the group of RCS; it figures as Case 1 in my material. In a couple of other cases the histologic diagnosis presented some difficulties, but their identity as cancers could nevertheless be established. As in Quick's and Cutler's material, the morphology in this group of tumors varied considerably. We have seen cases with uniformly rounded or oval cells, growing either in typical alveolar formations or more diffusely infiltrating, and others with a pronounced cellular polymorphism and an irregular manner of growth.

CLINICAL CHARACTERS OF RCS

Occurrence and Development.—The RCS are no uncommon tumors. Of our entire material of malignant tumors of the throat and lymphatic organs in the years 1929–1936, 150 cases in all, they constitute

roundly 11.5 per cent. Also, the statements of other authors indicate that they are of that relative frequency. Baumann-Schenker, of Zürich, who has a material of 60 cases of sarcoma of the upper air passages, finds among these six cases of RCS (10 per cent). The patho-anatomical material from the years 1933–1936, investigated by De Oliveira, contains no less than 20 cases. Eigler and Koch, of the Ear Hospital in Halle, observed eight cases during the years 1932–1935; and Gunsett, of Strasbourg, reports 21 cases for the period from 1922 to 1930. In the coming years, the number of cases of RCS reported will probably be very much increased.

Of my material, ten cases are male, eight female. Among the 38 autopsy cases from Roessle's institute mentioned by Roulet and De Oliveira, the female cases preponderate, however, with 57 per cent, as against 43 per cent of male.

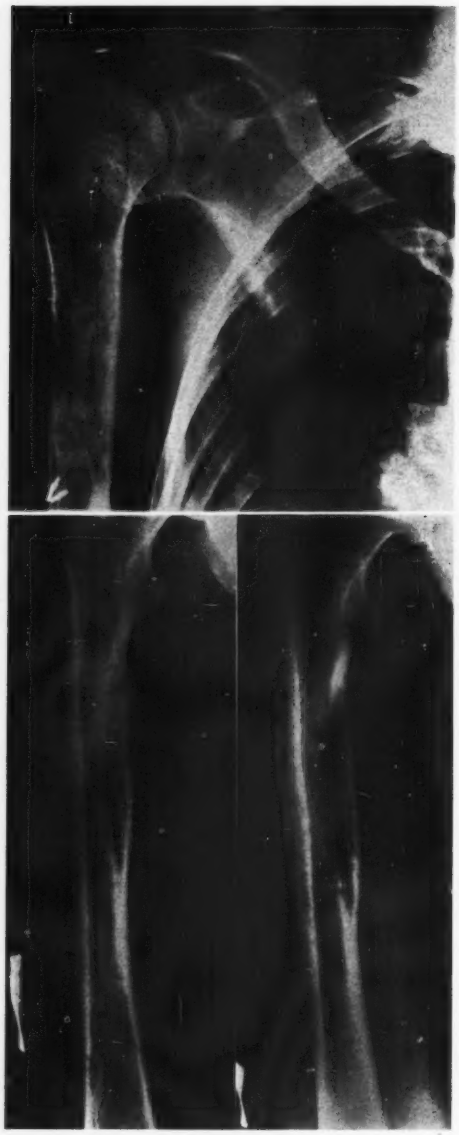
The *distribution according to age* shows in my material 11 cases between the ages of 51 and 70; two between 31 and 40; two between 41 and 50; and three over 70 years of age.

It is not easy from such information as is to be gleaned in the literature to get a precise idea of the time which it takes for these tumors to develop. In his first paper on the subject, Roulet thinks he may characterize them as relatively benign, noticeable for their slow growth, and late metastasis formation; but in his second paper he admits that also markedly malignant cases are to be found, especially among the tumors arising from the pharynx. Baumann-Schenker, whose material is too small, however, to make it of any value as basis for such conclusions, is of the opinion that RCS must be regarded as relatively benign. Eigler and Koch, on the other hand, lay stress on the markedly malignant character of their cases: and also Gunsett's material, as well as the case histories of the postmortem cases published by De Oliveira, seem to confirm that view.

My own material seems to me to show beyond doubt that the majority of RCS must be considered as being of a character extremely malignant, especially on account of their marked tendency to early metastasis formation. All my cases except four had manifest metastases when admitted to the hospital, most of them strongly developed. Table I shows the time elapsed in the different cases between the appearance of the first tumor symptoms, as stated by the patients, and their entrance into the hospital. It shows that three of them —Cases 4, 7, and 14—first noticed glands in the neck a month before their admission. When they were seen on entry, these had already grown into enormous glandular masses occupying the whole extent of the neck. In nine cases—Cases 1, 2, 3, 5, 6, 8, 9, 11, and 12—the history begins with the direct symptoms from the primary tumor in the nose or fauces. Of these, four were admitted within two months or less; two, within three months, and three, within four or five months. Case

TABLE I.—FIRST SYMPTOMS AND DURATION OF HISTORY BEFORE ADMISSION

Case	Tumors of Nasal Cavity and Epipharynx	Time	Case	Tonsillar and Pharyngeal Tumors	Time	Case	Tumors of Lymph Nodes	Time
1	Obstruction of nose; bleeding	1 month	7	Cervical node	1 month	14	Unilateral cervical nodes	1 month
2	Headache; mucous secretion	3 weeks	8	Swallowing troubles	2 months	15	Bilateral cervical nodes	3 months
3	Obstruction of nose	5 months	9	Swallowing troubles	3 months	16	Unilateral cervical nodes	6 months
4	Cervical node	1 month	10	Cervical nodes	4 months	17	Unilateral cervical nodes	4 months
5	Obstruction of nose	4 months	11	Obstruction of nose	3 months	18	Unilateral cervical nodes	3 months
6	Swallowing troubles	4 months	12	Swallowing troubles	6 weeks			
			13	Hoarseness	11 months			



(*a*) (*b*)

Fig. 8. Case 2 (*above*). Bone metastases of RCS in the scapula and humerus.

Fig. 9. Case 1 (*below*). Bone metastasis in the femur: (*a*) before and (*b*) after roentgen treatment.

14 was admitted with a recurrence following an extirpation of glands, performed in another hospital, and this recurrence had developed with lightning rapidity in the course of a few weeks. Making allowance for the negligence with which many persons treat their symptoms, when there are no pains, these facts seem to indicate a very rapid evolution. On the other hand, there are cases, though more rarely, in which the progression is slow. In Case 13, for instance, eleven months intervened between the occurrence of the first glandular metastases and the patient's admission; but in the meantime he had several times been treated with roentgen rays in another hospital, so that the present tumor was a recurrence. In Case 16, too, the patient had been going with her tumor for six months before she came to us.

The Gross Appearance of the Tumors.—The appearance of *epipharynx tumors* is only slightly characteristic. They usually form hard, knotty, easily bleeding masses of a more or less reddish color, which often fill the whole epipharynx, hinder the respiration by blocking the choanæ, or cause bleeding through compression of the tubal ostium, and sometimes pain in the ear region.

Primary tumors of the tonsils manifest themselves in the early stages as uniform swellings of the tonsil, whose external shape remains unchanged. The consistency is mostly firm, though softer than in cancer; the mucous lining is usually intact, the surface smooth or finely granulated. The color is usually darker red than that of the surroundings, and generally of a bluish-violet tint. *With increasing growth,* these tumors become very large and voluminous, block nearly the whole of the mesopharynx, and usually spread as a continuous growth upward into the epipharynx and downward along the lateral wall of the hypopharynx, eventually reaching as far as to the pyriform sinus. A noticeable feature is their tendency to infiltrate the surroundings, the soft palate, the pharyngo-palatine arches, and the root of the tongue, whereby the tumor becomes strongly fixed toward the depth. These large tumors ulcerate very easily, which results in the formation of deep, fissured craters surrounded

by excrescences and often coated with gangrenous necroses. In contrast to the RCS, the lymphosarcomas seem long to retain the form of the tonsil, and to have a smoother surface. Also, their ulcerations are less deep, and have rather the character of superficial, gray-coated mucosal defects (Berven).

Primary Lymph Node Tumors.—The five cases of these which I have observed were all localized to the lymph glands of the neck. With regard to the localization of RCS, in general, Roulet notes that they seem to have a certain predilection for the upper part of the body. His material, at the time when he made this observation, consisted exclusively of lymphoglandular tumors, only one of which was situated as far down as the groin. His opinion is fully confirmed by later publications, in which the great majority of tumors, just as in my own material, are seen to have originated in the upper air passages; whereby that predilection finds its natural explanation. Clinically, I have not been able to see any marked difference between the RCS primarily occurring in the lymph glands, and the regional lymph gland metastases.

The *metastases*, in the case of these tumors, occur as well along the lymph vessels as along the blood vessels. In the case of tumors of the pharyngeal cavity, the regional metastases often develop so early that their enlargement is the first clinical symptom noticed. In the very early stages, these glandular metastases are very little characteristic and are difficult to distinguish from tuberculous lymphomas or lymphogranulomatoses. In cases of slow development the glands may remain thus for a rather considerable time, solitary or multiple, displaceable and of limited size. In the majority of cases, however, the growth is very rapid; the process attacks the neighboring glands and infiltrates the surrounding tissues; reactive edemas develop, so that within a few weeks large concreted masses are formed, in which the palpating finger is no longer able to distinguish the individual nodes. In not a few cases there is an almost simultaneous development of bilateral glandular metastases, even though the primary tumor in the fauces is decidedly unilateral; and often the tumor spreads in a short time even to the axillary glands, which then readily attain the same size as the glands of the neck, or even larger. As long as the process of infiltration has not advanced too far, the consistency of the metastases is fairly solid, but not so hard as is usually the case in cancer. On the whole, the metastases in the case of RCS bear the definite mark of the mesodermal origin of the tumor.

Another marked characteristic of the RCS is their pronounced tendency to become *generalized*. This has been noted by all previous authors, and could in my material be demonstrated in five of the cases in which an autopsy postmortem was performed (Cases 2, 14, 15, 16, and 18). What particularly stamps the course of an RCS, clinically, as something fateful, is that such distant metastases not infrequently occur secondarily, long or shortly after the patient has been happily freed both of the primary tumor and any existing regional metastases, and without any recurrence having set in at the sites thus treated.

In the following I have attempted to sort out *different clinical types* of metastases from my material. The largest number of cases, namely, Cases 3, 4, 5, 7, 10, 11, and 15, show—so far as it has been possible to trace—metastases only to regional and distant groups of lymph glands. In five cases, namely, Cases 13, 14, 16, 17, and 18, metastases occurred first in regional and distant glands, in a later stage also in internal organs. Cases 1, 2, and 6 are characterized by metastases to the skin and subcutaneous tissues, and in Cases 1, 2, and 13 there are numerous metastases to the skeleton, of a purely destructive type.

With regard to the origin of the *tumors in lymph glands*, Ahlström says that usually it is not a single gland alone that undergoes a blastomatous transformation, but that the process begins in several nodes at the same time. This should be due to a multicentric genesis of the RCS—a tendency to

involve the system by simultaneous attack on parts of tissue belonging to the same functional unit. He would see in this the indication of a possible relation to the generalized reticuloses.

When the generalization of an RCS has once begun, the process may thus attack almost any organ. In my material, metastases have been demonstrated in mediastinal, retroperitoneal, and mesenteric lymph glands; in the liver, spleen, pancreas, and bone marrow; in the mucosa of the digestive tract; in the lung tissue, the renal parenchyma, and the testicles; finally also, in subcutaneous tissues, the musculature, and the skeleton. Histologically, the metastases are everywhere characterized by destruction of the normal tissues, and the substitution of the latter by the typical reticular-cell syncytium.

I have not in my material been able to ascertain *primary blood changes* of any magnitude, except in Case 2, which showed a typical lymphatic leukemia of chronic character, with 428,000 white blood corpuscles, 97 per cent of which were lymphocytes.

THERAPY

It goes without saying that a type of growth with such malignant characters as those of RCS is in every way unsuitable for surgical treatment. The large risks of an operative intervention are illustrated, for instance, by my Case 14, in which large local recurrences developed within a few weeks after extirpation of the primary lymph node tumor. Eigler and Koch, also, report two cases of RCS of the tonsil, in which extirpation was done because carcinoma of the tonsil was suspected (*sic*). In both cases the result was immediate recurrence and the death of the patient. Of course, not even a biopsy should be done unless there is a possibility for subsequent rational treatment.

By *rational treatment* I mean in these cases *radiation treatment*, a therapy indicated specially on account of the great radiosensitivity of these tumors, which has been ascertained by all the authors who have studied them, and which has also been noticeable in my material. Both the primary growths and the metastases to lymph glands and organs possess this quality, and even on irradiation of bone metastases we have observed a distinct effect in the form of new formation of bone and sclerosis. The radiosensitivity is not so striking, however, as that of lymphocytomas, for instance, and the doses required for producing a clinically noticeable effect on an RCS are markedly higher. Nevertheless, radiation therapy is the only method by which there is at present any prospect of obtaining lasting freedom from symptoms in these tumors, because, if properly employed, it may influence at the same time the primary tumor and the nearest glandular regions. Also, in cases of incipient generalization the irradiation can check the development of the process, at least to a certain extent. On all this, I believe, there is no difference of opinion; but on the other hand, a review of the literature shows that different radiologists have chosen different methods of radiation, and also that in favorable cases a good result may be obtained in different ways.

In the radiologic clinic in Lund I have used, as a principal method, simple fractional roentgen, with a secondary tension of 165–170 kv., 6–7 ma.; focus-to-skin distance 40–50 cm. With these factors, and with a filter of 0.5 mm. Cu + 1 mm. Al, our apparatus gives us, respectively, about 35 and 25 r/min.: with Thoraeus' tin filter, respectively, about 15 and 10 r/min. In the first years, when we were not so familiar with the biological characters of RCS, we gave short series of treatment, with relatively large single doses of the roentgen ray. The results were on all points inferior to what we have obtained later since we began to use a more regularly fractional treatment with smaller daily doses—on the average 150–200 r—and spread the full treatment over at least two and a half or three weeks. The total dose to each portal has varied between 900 and 2,500 r, but should not be less than 1,500 r, divided into eight to ten single doses to each portal. With

this technic there is great prospect of obtaining permanent healing both of primary tumors in the fauces and nasal cavity, and of any possibly existing regional metastases.

The *protracted roentgen treatment, ad modum* Coutard, which, for instance, in Schinz' institute is employed routinely also for RCS, we have not been able to use because of lacking facilities.

On the other hand, we have in two cases used *teleroentgen treatment* (the longest focus distance which we are able to employ in our present x-ray department is 120 cm.), either in the form of irradiation of the trunk *in toto* (Case 16; the treatment, only begun, was interrupted by the death of the patient), or with the body marked off into several large portals and serial irradiation *ad modum* Mallet (Case 1). This method seems to give satisfactory results, and may be recommended on probation for suitable cases.

In a few cases, *radium* has been employed to complete the treatment. In five cases, in which remnants of the tumor remained, we used *teleradium*, but without obtaining any better result than with the roentgen ray. In two cases, *local application of radium* was used as a complementary technic with good result in the epipharynx and the tonsillar region. A routine combination with local radium application, similar to Berven's technic for sarcoma of the tonsil, we have not deemed necessary, considering the great improvement that may fairly be counted on from the roentgen treatment alone, when carried out according to the fractional dosage technic.

The following tables will show the results of our treatment. It is evident that there cannot be any question of five-year results, as the material is from the period 1929–1936, and most of the cases have so far been followed up only for a few years. As far as RCS is concerned, however, every single case observed is of interest; and I have, therefore, not hesitated to include even a couple which were treated as late as in the beginning of this year.

Four cases (4, 9, 11, and 12) remain free

TABLE II.—CASES SYMPTOM-FREE

No.	Pat.	History	Primary Tumor	Metastases	Treatment	Immediate Results	Clinical Course	End-results	Duration of Life
4	I. J., woman, 61 years	1 month (Dec. 6, 1935)	Epipharynx total; P.A.D.; fibrillar type	Bilateral fixed nodes of neck and axillæ	Fractional roentgen	Symptom-free	No recurrence	Alive; symptom-free	1 year, 4 months
9	A. K., man. 33 years	3 months (May 14, 1931)	Left tonsil; P.A.D.; fibrillar type	Diffuse lesion of nodes, left neck	Fractional roentgen	Symptom-free	No recurrence	Alive; symptom-free	6 months
11	J. H., man. 75 years	3 months (Oct. 19, 1934)	Left tonsil; P.A.D.; fibrillar type	Fixed nodes, left neck	Fractional roentgen	Symptom-free	Axillary recurrence; treatment; symptom-free	Alive; symptom-free	2½ years
12	J. L., man, 70 years	1½ months (Jan. 18, 1937)	Left tonsil; P.A.D.; fibrillar type	No metastases	Fractional roentgen	Symptom-free	No recurrence	Alive; symptom-free	6 months
6	J. N., woman, 70 years	4 months (March 24, 1936)	Back wall of epipharynx; P.A.D.; fibrillar type	Bilateral cervical nodes, movable	Fractional roentgen; local radium application	Symptom-free	Metastases of subcutis, both arms; treatment	Alive; symptom-free(?)	1 year, 2 months

TABLE III.—CASES DEAD DURING FIRST TREATMENT

No.	Pat.	History	Primary Tumor	Metastases	Treatment	Immediate Results	Clinical Course	End-results	Duration of Life
10	P. J., man, 67 years	4 months (March 1, 1932)	Both tonsils, preferably right; P.A.D.; polymorphocellular type	Bilateral cervical nodes, movable	Roentgen; teleradium; treatment interrupted	Improved	Heart failure	March 23, 1932, bronchopneumonia	3 weeks
15	K. P., woman, 68 years	3 months (July 5, 1933)	Bilateral cervical nodes; P.A.D.; polymorphocellular type	Mediastinal nodes, Liver	Roentgen; interrupted treatment	Lung embolism		July 6, 1933, lung embolism	1 day
16	B. A., woman, 66 years	6 months (Dec. 2, 1933)	Cervical nodes, right side; P.A.D.; fibrillar type	External lymph node regions; P.A.D.; fibrillar type	Roentgen; total irradiation; interrupted	Not improved; asphyxia	Distant metastases; cachexia	Dec. 20, 1933, cachexia	3 weeks

from symptoms, having been followed up through, respectively, six, two and one-half, one and one-half years, and six months. Case 6 has shown, after freedom from symptoms for one year, beginning metastases in the subcutis of the arms, which now are being treated. On the whole, the experience with this material shows that in RCS recurrences and metastases usually occur considerably earlier; that is, at the latest, six months after the treatment. There is thus some reason to suppose that the four cases above named will continue to remain free from symptoms.

Three patients died while the treatment was yet in progress; one from pulmonary embolism, one from bronchopneumonia, and one because of distant metastases (Cases 10, 15, and 16).

In four cases death supervened owing to local recurrences or persisting tumor remnants which progressed afresh after treatment. In all these cases the treatment must be said to have been insufficient or the technic employed unsuitable (Cases 3, 7, 8, and 17).

Case 14 was a local recurrence following operation, and its prognosis was particularly bad. The patient died with generalized metastases after a few months. Also, in this case the technic was altogether unsatisfactory.

Cases 1, 5, 13, and 18 died with distant metastases relatively long—7 to 18 months—after the beginning of the treatment. The last three named of these patients (Cases 5, 13, and 18) were at the time of their death still free from both local and regional symptoms. Case 1 shows a curious course, with repeated recurrences and metastases, chiefly to the subcutis, the testicles, the nasal cavity, and the skeleton.

Finally there remains Case 2, which was complicated with lymphatic leukemia, the symptoms of which can perhaps be traced back in the case history for about a year. The course of this case was extremely rapid, the patient dying only one month after beginning of the treatment, though both leukemic and the sarcomatous changes seemed to indicate a strong effect of the

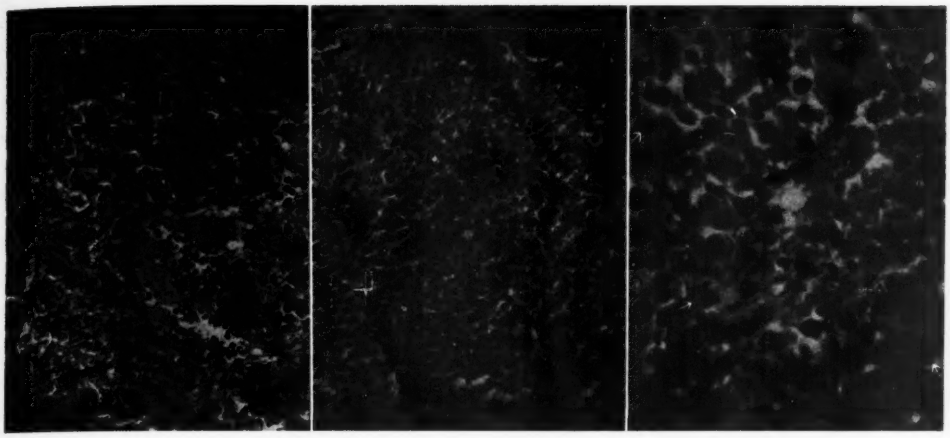


Fig. 10. Fig. 11. Fig. 12.

Fig. 10. Case 2. RCS associated with lymphatic leukemia.
Fig. 11. Case 20. Generalized reticulosis. Section from skin infiltration in the groin.
Fig. 12. Case 19. Generalized reticulosis with numerous mitoses (see arrows).

treatment. Which one of the two pathologic factors was determining for the final issue it is impossible to decide with any certainty.

The results now reported will probably, in the eyes of most observers, seem rather poor, and so they are from a general standpoint. However, the results of a therapy are in a high degree dependent on the character of the material. In this respect, I wish to call attention to the well-known fact that, in radiotherapy, such tumors as show the most marked radiosensitivity very often will give bad results as to the possibility of permanent cure. This proves true also with RCS and depends without doubt on their tendency to form metastases, both regional and distant. The results published by other authors (Gunsett, Koch, and Eigler) bear the same stamp of the impending danger of generalization of the process, whereby the expectation awakened by local healing too often is frustrated. There seems to be no other help for this difficulty than increased efforts from the organization to make the patients seek assistance as early as possible.

At last, some words on the two cases of *generalized reticulosis* above named. According to Oberling and Guérin, this diagnosis ought to be reserved for cases in which the pathologic process cannot be defined but as proliferative phenomena in the reticulo-endothelial cells that constitute their main histopathologic substratum. These demands are altogether answered by both cases, though between them there exist great differences.

In Case 19 (female, aged 58 years) the history of development is very short, the malady arising from the axillary nodes and in a few weeks spreading to the other external lymphatic regions. The upper air passages were not involved; the liver was enlarged, but not the spleen. There was a moderate anemia with a light monocytosis. Roentgen treatment had a good immediate effect, but in a very short time a new gland tumor appeared in the epigastrium, and the liver increased. Renewed treatment was tried in vain, and in a couple of months the process led to death.

Case 20 (female, aged 46 years), on the contrary, has a markedly chronic course. Seven years ago the glands of the left groin began to swell; two years later those of the right side also were involved. One year ago, there appeared an infiltration of the skin of both inguinal regions in the shape of hard, reddish-brown tumors, rather closely

TABLE IV.—CASES DEAD FROM PERSISTING TUMORS OR LOCAL RECURRENCES

No.	Pat.	History	Primary Tumor	Metastases	Treatment	Immediate Results	Clinical Course	End-results	Duration of Life
3	A. N., man, 45 years	5 months (Feb. 5, 1932)	Right side of epipharynx; P.A.D.; type unknown	Bilateral cervical nodes, movable	Fractional roentgen; teleradium	Symptom-free	Local recurrence, not treated; cachexia	*Oct., 1932, from local recurrence	8 months
7	J. O., man, 57 years	1 month (April 10, 1929)	Both tonsils, preferably right; P.A.D.; type unknown	Fixed nodes, right neck and left axilla	Fractional roentgen	Improved not symptom-free	Progression	*July 21, 1929, general cachexia	3 months
8	A. P., man, 56 years	3 months (May 13, 1931)	Right tonsil; P.A.D.; polymorpho-cellular type	Fixed cervical nodes, right side	Fractional roentgen; teleradium, local radium	Not quite symptom-free	Local recurrence, treatment; lymph gland dissection	*Feb. 9, 1931, distant metastases; cachexia	9 months
14	A. S., man, 37 years	1 month (Dec. 18, 1929)	Recurrence of cervical nodes (operated on); P.A.D.; fibrillar type	Bilateral axillary nodes	Fractional roentgen	Not quite symptom-free	Distant metastases; treatment	*Aug. 4, 1930	8 months
17	P. O., woman, 71 years	4 months (Aug. 2, 1935)	Cervical nodes, left side; P.A.D.; type unknown	Cervical nodes right side	Fractional roentgen	Improved	Local recurrence	*Oct. 20, 1935, local and distant recurrences	2½ months

* Signifies that patient died.

resembling keloids. On admission in February, 1937, the process had spread also to the axillary glands and there was a light anemia. The upper air passages and inner organs were not impaired. A fractional roentgen treatment brought about a nearly complete vanishing of the gland tumors and skin infiltrations, which were replaced by fibrosis. Later on, however, beginning impairment of the general condition, increased anemia, and fresh nodes in the neck showed that the malady was proceeding and had a systemic character.

In both cases, the histologic diagnosis was *reticulosis*. In the literature, I have not found any descriptions of such skin infiltrations as described above in reticulosis. In both cases, the reticular syncytium had a typical, uniform aspect with a tendency to formation of an intraplasmatic fibrillary network.

In fact, the clinical prognosis with generalized reticulosis seems to be as bad, if not worse, than in generalized RCS. Although the malady may in some cases take a mild and protracted course, anemia and cachexia will gradually predominate. Histologically, also, there are changes suggesting that the limits between these two related conditions often cannot be sharply drawn. Thus, in Case 19, although the character of a uniform reticulo-cellular hyperplasia preponderated, we found rather numerous mitoses and in some places also a very thorough transformation of lymphatic tissue into a reticular syncytium. On the other hand, certain cases of RCS (for instance, my Case 18) have revealed systemic reticulo-cellular formations of such a character that the pathologist has hesitated as to

TABLE V.—CASES DEAD FROM DISTANT METASTASES WITH PROTRACTED COURSE

No.	Pat.	History	Primary Tumor	Metastases	Treatment	Immediate Results	Clinical Course	End-results	Duration of Life
1	B. J., man, 63 years	1 month (May 14, 1935)	Left maxillary sinus, nasal cavity; P.A.D.; undifferentiated	No metastases	Fractional roentgen teleradium	Symptom-free	Metastases to the testes, skeleton, subcutis, muscles; local recurrences of nose; treatment; renewed recurrences	*March 8, 1937; distant metastases, cachexia	1 year 9 months
5	M. P., woman, 59 years	4 months (March 9, 1936)	Back wall of epipharynx; P.A.D.; fibrillar type	Bilateral cervical nodes; left axillary nodes	Fractional roentgen	Symptom-free	Distant abdominal metastases; treatment	*Oct. 11, 1936; general cachexia	7 months
13	J. E., man, 70 years	11 months (Nov. 30, 1933)	Left wall of hypopharnyx; P.A.D.; fibrillar type	Left cervical nodes, movable	Fractional roentgen	Symptom-free	Distant metastases to lymph nodes, colon, skull; protracted course	*Dec. 21, 1936; metastases, cachexia	3 years 1 month
18	A. J., woman, 31 years	3 months (Sept. 23, 1935)	Right cervical nodes, tonsils(?); P.A.D.; fibrillar type	No metastases	Fractional roentgen	Symptom-free	Distant metastases; treatment; protracted course	*Nov. 8, 1936; cachexia and uremia	14 months

*Signifies that patient died.

TABLE VI.—CASE ASSOCIATED WITH LEUKEMIA AND TWO CASES OF GENERALIZED RETICULOSIS

No.	Pat.	History	Primary Tumor	Metastases	Treatment	Immediate Results	Clinical Course	End-results	Duration of Life
2	J. L., man, 75 years	3 weeks (Jan. 11, 1937)	Left nasal cavity; P.A.D.; fibrillar type; lymphatic leukemia (associated)	External lymph node regions	Fractional roentgen	Regression of tumor and leukemic blood changes	Cachexia	*Feb. 12, 1937; cachexia	1 month
19	M. H., woman, 58 years	5 weeks (April 20, 1935)	Left axillary nodes; P.A.D.; reticulosis, fibrillar type	External lymph node regions	Fractional roentgen	Improved; decrease of nodes	Internal and external metastases	*Aug. 4, 1935; cachexia	$3^1/_2$ months
20	J. J., woman, 46 years	7 years 5 years 1 year (Feb. 15, 1937)	Left inguinal nodes; right inguinal nodes; skin lesions; P.A.D.; reticulosis, fibrillar type	Right axillary nodes	Fractional roentgen	Improved; regression of nodes and skin lesions	Metastases left cervical nodes; treatment	Alive, in treatment	6 months

*Signifies that patient died.

whether he should diagnose a reticulosis or a reticulum-cell sarcoma (RCS).

The more cases of disturbances of the reticulo-endothelial system become known and are described, the stronger is the impression one gets of the numerous varieties and transitions existing between the special types that are published.

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BASIC PRINCIPLES FOR SUCCESSFUL ROENTGEN THERAPY OF CARCINOMA

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THE value of radiotherapy certainly is not disputed any longer, but its execution is very difficult and should be based on thorough knowledge and personal experience. Therefore, it is easy to understand that results are not equally satisfactory in all the clinics where roentgen rays are used. It should be added that those who pass an unfavorable judgment have only a very superficial knowledge of radiotherapy; they usually ignore the physical foundations as well as the biological actions of the rays. The application of roentgen rays is an art to be learned and practised just as the art of surgery. Results will never be favorable in places where a patient, suffering from cancer, is sent to the roentgen room to be treated by a non-medical personnel.

The possession of a modern roentgen machine is not the only or most important prerequisite of successful roentgen therapy, surprising as such a statement might still be to some illogically thinking medical and non-medical persons. Certainly, any surgeon would be offended if somebody would dare to attribute his good results exclusively to his well furnished surgical amphitheater or to his modern instruments. However, the results a roentgen therapist obtains by his treatment are attributed too frequently to nothing other than his modern equipment.

To be sure, the best machines and accessories constructed to-day are none too good for serious roentgen therapeutic efforts; in fact, we still lack machines which operate continually with precision, thus reproducing, without fail, rays of identical characteristics and quantity.

Present-day apparatus cannot be left to work independent of control. Obviously, operators of such machines must be thoroughly aware of their physical and technical deficiencies. They must also have a sound knowledge of the physics of roentgen rays, for one of the most difficult problems of roentgen therapy is correct dosage.

Though we speak to-day of an international roentgen unit, designated by "r," an outsider only could be of the opinion that the application of this dose, its reproductability and, last but not least, its exact scientific determination, are simple measures. The statements of many papers, that a certain number of r units has been applied, are useless, if prevailing biological and physical conditions are not recorded correctly—and in detail.

Knowledge of the exact physical characteristics of roentgen therapy is of the same importance as that of the medical and biological characteristics.

I emphasize my conviction that both are equally important, as there are still quite a number of authors who attribute failures to faulty biological reaction of the organism instead of recognizing their own roentgen therapeutic shortcomings. Nature itself, through a different radiosensitivity of body cells, provides the basis for all radiotherapeutic attack on cancer. Here I must dispose of an old error, which, though corrected long ago and often, still reappears in the literature from time to time, regarding the conception of radiosensitivity: *There is no "elective" radiosensitivity.* The assumption of such an electivity has caused some of the most disastrous effects during the past twenty years. Experience has shown that all the cells in the body are affected, and none are immune to destruction by roentgen rays.

The possibility of efficient cancer therapy, therefore, is based upon the fact that cancer cells are more radiosensitive than normal cells. But this postulate should be

understood *cum grano salis*, as the radiosensitivity of the cells of ovarian follicles, the cells of lymphatic glands, of spleen, of blood, and of the intima cells of blood vessels is appreciably higher than that of some cancer cells.

Another error should be mentioned here: radiotherapy is a local measure, first and last. The action of rays on the general organism and its defense mechanism is of minor importance. Therefore, the primary effect of the roentgen rays is the destruction of cancer cells locally. The old opinion that roentgen rays stimulate the connective tissue to the extent of strangulation of the cancer cells is erroneous. Neither can the general defense of the organism be stimulated to dissolution of cancer cells by any type of proteolysis, nor products of disintegration of cancer cells produce disappearance of tumors.

The surgical extirpation of a cancerous tumor is justified only if one adopts the point of view that cancer, at the onset, is a local disease. Those believing that newgrowth is only a symptom of a systemic cancerous disposition cannot expect a local measure, such as a surgical operation, to be successful.

The same applies to radiotherapy, which, too, is a local measure. The action of the roentgen rays, however, reaches appreciably farther than that of the bistoury.

Though we assume that cancer is a local disease at the start, we do not dispute the statement that constitutional factors play a certain rôle in its genesis. However, it is not necessary to postulate that wide fluctuations in its dissemination throughout the organism are induced exclusively by systemic disposition; the original site of the newgrowth, its relation to the surrounding tissues and, very frequently, medical interference favoring dissemination, suffice to give a satisfactory explanation for the spreading of cancer. Beside, newgrowth is favored not only by a good blood supply of the affected part, but also by a well-developed lymphatic system.

It has been proved long ago that roentgen rays have a local action, which is limited strictly to their beam. If a dose necessary for the destruction of carcinoma were applied to one portion of a tumor only the typical subsequent alterations of cells could be seen only in this radiated area, while the other part of the tumor not radiated would show no signs of regression. On the other hand, the claim is undoubtedly justified that there are available quite a number of most promising measures, which accelerate resolution of a properly radiated cancer, as, for instance, medication of endocrine preparations.

In the problem of roentgen cure of cancer, two important phases should be recognized:

1. Destruction of the localized growth, together with detoxication and elimination of cell débris.
2. Repair at the site of the destroyed neoplasm by normal tissue and compensation for the damage created in the organism by the tumor, its toxins, and also by the roentgen rays.

The term "destruction" should not be conceived in its narrowest interpretation, conveying the implied idea of a sudden effect. Proper radiation does not induce such a sudden effect, as it results, for instance, from thermocauterization; this procedure alters the tumor immediately and most visibly, so that the cells appear to be damaged distinctly. In the case of a well-directed roentgen radiation, however, one does not see any immediate macroscopic change, nor can one find microscopically any *specific* alterations, even after a delay of a few days.

(The pronounced alterations of cells brought about by radium are due to extreme over-dosage, a "caustic effect.")

The point of attack of the roentgen rays in the cell is the nucleus. Cells are most radiosensitive in the karyokinetic stage. Any tumor, of course, contains cells in various developmental stages; consequently the action of an exactly measured dose of rays on cells in different conditions varies.

If a tumor has received a very high dose

of roentgen rays, a "caustic dose," one soon can observe severe hyaline degeneration, pyknosis, and keratolysis. The use of such high doses in practical roentgen therapy would be absurd. The highest permissible dose is one just sufficient to inflict lethal injury to quiescent cancer cells. With the employment of such relatively small doses, about three weeks have to elapse usually before a diminution of the tumor can be observed macroscopically. Only cells in the karyokinetic stage have perished immediately after roentgen treatment. The rest of the cells continue to live up to the moment of their karyokinesis. Cells which have been in a state of complete rest at the time of radiation have suffered the least severe injury; they are able to undergo karyokinesis once or twice, but after that, their regenerative function is extinct. If one desires to apply to the action of the roentgen rays on a cancerous tumor one single descriptive term, one might speak of "castration" rather than of "destruction."

The reason for application of the smallest curative dose for the elimination of cancer is the necessity to spare the surrounding tissue as far as this can be done; for, after the dissolution and death of the cancer cells, young bands of connective tissue are to replace the former strands of carcinoma.

The dose necessary for successful treatment of cancer has been determined long ago and has been tested in numerous cases. We have called this quantity of rays "cancer dose" (Ca-D). It has been expressed in physical terms and by establishment of a relationship between electrophysical units and a biological phenomenon. Knowing that the first impressive reaction following application of a certain amount of roentgen radiation is an erythema, we have correlated it to this reaction manifest in the skin. If the dose is increased, desquamation occurs and even caustic destruction. We designate as "skin unit" that quantity of rays which produces a marked reddening of the skin after from eight to ten days, and after from four to six weeks a faint tanning, often lasting for years. This reaction of the skin is rather constant. There are no material variations between representatives of various races. This "skin unit," as determined electrometrically, includes a biologic variation of ± 10 per cent.

We relate other biological measuring to the "skin unit" in order to form a conception concerning the reaction of individual cells, but, we also record the magnitude of the various doses in the international unit, "r".

The dose necessary for arrest of the menstrual cycle is the "sterilization dose," which amounts to 34 per cent of the "skin unit"; it means that about one-third of that single quantity of roentgen rays which is tolerated by the skin without permanent damage is sufficient to destroy the highly radiosensitive cells of the ovarian follicles.

We have found the "cancer dose" to be from 90 to 125 per cent of the "skin unit," the dose of 90 per cent representing the lowest permissible limit, not to be reduced if one expects to exert a curative action on a cancerous growth. During the last ten years we have always employed at least 110 per cent of the "skin unit" in the treatment of any carcinoma; for the adenocarcinomas we even raised the amount to 125 per cent. In biological terms, these values mean that with application of 110 per cent of the "skin unit," the skin responds with a pronounced reddening and even with a marked swelling of the follicles, while 125 per cent of the "skin unit" brings about vesiculation and subsequent desquamation.

One may deduct from these statements that it is by no means easy to apply in the depth of the body a dose which is necessary to destroy cancerous growth.

The intensity of the roentgen energy, which we project into the body, is gradually reduced by absorption and by distribution over larger areas at increasing distances, according to the well-known inverse square law: at a focal skin distance of 30 cm. we obtain in a depth of 10 cm. a dose of 22 per cent of the surface dose. Therefore, we must radiate a cancerous tumor lying at such depth through several ports in

order to obtain by summation 110 per cent of the "skin unit" dose at the site of the tumor. In case of a tumor growing on the surface, sufficient concentration of radiant energy by the use of several portals of entry may at times prove nearly impossible. As the loss by absorption is fixed for given potentials and filtration, we must then attempt to reduce the inhomogeneity of intensity in such a superficially located area by other compensations. For instance, we choose a long focus-skin distance in treating breast cases, performing the irradiation from a distance of 100 to 120 cm. It would lead too far to enter into the discussion of the technical difficulties which arise as soon as we try to apply the cancer dose to various parts of the body, but I would like to say a word about the following locations: in a case in which a cancerous growth is situated in the center of the abdomen, as, for instance, a cancer of the uterus, one can adjust portals of entry in the form of a girdle, thus obtaining the necessary concentration in the depth. In anal cancer situated near the surface and surrounded by most uneven body levels, we often have to be satisfied with roentgen irradiation from one external perineal port and have to rely on a combination of roentgen rays, with radium for completion of the cancer dose throughout the neoplasm. Considering these difficulties of dosage, it is not astonishing that the results are very unsatisfactory in cancer of the anus, but they are much better in cases of cancer of the rectum situated about 12 to 15 cm. higher up. Its site in the center of the body is similar to that of a cancer of the uterus, so that it is relatively easy to apply the necessary dosage. Still more striking is the difference between the results obtainable in cancer of the cervix uteri and those in vaginal and vulvar cancer. In these cases we have to deal with the same histological type of cancer, *i.e.*, a squamous-celled epithelioma. But while we obtain five-year cures in about 70 per cent of the cases of cauliflower tumors of the vaginal portion of the cervix uteri, as long as the cancer is limited to the cervix, the results are quite unsatisfactory in cases of vaginal cancer, in which roentgen therapy yields only 25 per cent of cures, about the same percentage as in cases of cancer of the vulva.

One might interject that the cancer of the cervix, which grows exophytically, is limited to its focus for a relatively long time, while, on the contrary, the cancers of the vagina as well as those of the vulva spread more rapidly into remote lymphatic channels, favored by wide lymphatic communications. I admit that these biological conditions play an important rôle with regard to the extension of cancer, but the differences in the results would not be so great if application of a proper carcinoma dose were easier. In cases of vaginal cancer, application of the cancer dose to the whole length of the vagina is not possible readily, because the intensity of a beam entering through a vulvar field diminishes rapidly toward the depth. Suprasymphyseal ports, on the other hand, project insufficient intensities to the lower parts of the vagina. Therefore, an additional dose of radium is necessary in vaginal cancer, while in cancer of the cervix we can do without such.

It is also important to know that cells become resistant to the action of roentgen rays, in case they survive a sublethal dose.

It has been proved long ago that regression of a carcinoma by radiation can be induced only with a true "carcinoma dose" as designated above. Nobody has ever observed a case of genuine cancer responding with regression to the application of small quantities of roentgen rays. In such purported cases of the older literature, an error in measurements seems to have occurred.

If we apply a small sublethal dose, the cancer cell is damaged, but this injury is repaired more or less rapidly. This same reaction will occur in all cells influenced, but the rapidly growing cancer cell with its high metabolism, is fitted better for such repair than a cell of the connective tissue stratum.

The extent to which cutaneous cells are able to recover from damage inflicted by

small doses can be demonstrated easily by the following experiment. A carefully measured "skin unit" is applied to two nearly identical small fields, perhaps one on each thigh; if, to the one this dose were applied at one sitting, to the other, however, in five sittings on subsequent days, 20 per cent at a time, the difference between the biological reactions would be striking. While the first area, irradiated at one sitting, would show the typical reaction to the "skin unit" with a marked tanning after six weeks, the second area, which had received the "skin unit" in the course of five days, would scarcely show any perceptible response. Thus, the reaction to such a fractionated dose corresponds to the effect of 80 per cent of the "skin unit" in a single application. In order to obtain by fractionated doses a reaction equivalent to that of the "skin unit" applied at one sitting, one has to increase the total amount in a certain ratio to the fractionation employed.

Such experiments show that scattering of a full dose entails reduction of its biological efficiency. Therefore, if one is compelled to distribute the necessary dose over several days instead of giving it at one sitting, one should compensate for the loss caused by the recuperative faculty of the cells by the application of the so-called "additional biologic dose." A similar diminution of the biologic efficiency becomes manifest, if one increases the distance between target and body in order to gain a more homogeneous depth dose; it is then not sufficient simply to calculate the time according to the inverse square law, but in order to obtain the same biologic effect an additional dose is necessary, which in case of a change from, for instance, 30 cm. to 100 cm., should amount to 30 per cent of the calculated time.

This phenomenon of cell recuperation after application of sublethal doses explains why such high total doses are tolerated by those subjected to Coutard's method of treatment.

At first glance it seems to make no difference whether one applies a dose at one sitting or distributes it over several days, if only due allowance is made for the recuperative faculty of the cells. But it really is not the same, for cell recovery depends on the tolerance of the individual cells, and this, in turn, chiefly on their quite variable metabolism. The rapidly developing carcinoma cell is more radiosensitive, but on the other hand, it heals reparable injury more quickly. Cells of the connectivum, on the contrary, have a low radiosensitivity; however, they cumulate small doses to a higher degree than cancer cells.

In this type of tissue, therefore, the total effect of a fractionated dose is more intense than that of an equally large single amount of energy. One can express this experience also as follows: the ratio of radiosensitivity is altered by fractionation. The cancer cells become less radiosensitive; the cells of the connectivum, on the other hand, become more radiosensitive. But such a result is undesirable, for we should try to limit damage to the cells of the connectivum as much as possible, while cancer cells should be radiated by a dose guaranteeing their destruction. This is possible only by irradiation at one sitting. I think that all speculation with regard to Coutard's method is erroneous.

The opinion is held by some authors that by distribution of the dose over from ten to twenty days, the effect of roentgen treatment would approach that of radium therapy. But one overlooks the fact that the real difference in the effect of radium and roentgen rays is the lower absorbability of radium rays; in other words, that their penetrating power is greater than that of roentgen rays, even with allowance for the Compton effect. This valuable quality of the radium rays cannot be obtained by fractionation and protraction of roentgen energy. There are now available for comparison sufficient data in publications reporting the results produced by my method of single dose radiation and by that of Coutard. The comparison is in favor of my method.

Two characteristic mistakes frequently

account for failure of roentgen therapeutic efforts in cancer treatment:

1. Application of dosage insufficient for destruction of cancer cells because of ignorance of the biologic recuperative capacity of these cells.
2. Such cumulation of radiation that not only the neoplasm is destroyed, but also severe injury is inflicted to surrounding healthy tissue, the biologic radiosensitivity of which has been increased simultaneously so that it is no longer able to repair the defect.

Concomitant inflammation has an influence similarly unwelcome to that of fractionated doses. It is to the credit of Regaud and his collaborators to have shown the deleterious action of inflammation in cases treated by radium. Subsequently, we proved experimentally that relative radiosensitivity is altered by a coincident inflammation. The cancer cells become less radiosensitive, while the susceptibility of the surrounding healthy tissue is increased. For this reason, infected carcinomas may not regress if a dose of 110 per cent of the "skin unit" is applied, which, under normal conditions would be efficient. But if the dose is increased, there is danger of damage to the healthy surrounding tissue.

In order to avoid failures in cases of infected cancer, it is necessary to reduce the inflammation before radiation, as far as that is possible. It is not easy to obtain a satisfactory result quickly. Besides, one dare not lose too much time with disinfection measures, while the growth continues its development.

In cancer of the uterus, douches with rivanol and chinosol are useful, but by far the best results are obtained by our copper treatment on account of its deeply penetrating disinfecting action. The technic is the following: by means of a special electrode serving as the anode, the introduction of a solution of cuprum selenicum is induced. Thus, particles of copper and copper salt are incorporated into the tumor by iontophoresis.

Though it has been proved that these measures are useful, inflammatory carcinomas, indeed, offer a less favorable prognosis with regard to a permanent cure.

I referred above to failures caused by a dosage insufficient to bring about complete destruction of the tumor. It is necessary that the required dose be applied not only to the primary tumor, but also to the whole lymphatic region involved. This is not always possible, as there may be cases in which the full dose cannot be given over the whole region and others in which healthy tissue is damaged by over-dosage.

The task we undertake in treating cancer is not finished when we have applied the correct dosage. In order to secure satisfactory results by roentgen treatment, a systematic after-care should be employed.

The decomposition of cancer cells liberates toxins; besides, the organism is also loaded with products of metabolism produced by normal cells which have undergone the exposure to roentgen rays. This toxicosis becomes manifest as roentgen sickness (*Röntgenkater*) immediately after the irradiation. In most cases this symptom passes quickly, but there is many a patient suffering from this intoxication for some time. Therefore, it is necessary to control elimination before beginning irradiation; the function of the kidneys should be stimulated and the evacuation of the bowels taken care of. As a momentary measure of relief in cases of roentgen sickness, the intravenous injection of hypertonic solutions is employed at my clinic; later on, a rich supply of fluids is recommended, in order to cleanse the organism; last but not least, diuresis should be stimulated. For several weeks after radiation we give intravenous injections of colloidal sulphur, because the elimination of albumin débris is facilitated if there is an abundance of sulphur in the organism. We also prescribe sulphur *per os*, tending to improve elimination. A stay in high altitudes has a favorable effect, because a difference of 1,000 meters increases metabolism. Thus, all débris is eliminated

rapidly, the patient recovers more quickly and without complications.

Local treatment of the radiated parts is also necessary. As the radiated skin produces little oil, ointment should be applied carefully to it. The intestinal mucosa too, recovers more quickly from the effects of radiation by roentgen rays if oil instillations are given frequently.

As to the after-care of the radiated cancerous tumor itself during the period of decomposition and regression, it should be regarded as a *noli me tangere.* Regression should not be disturbed by any measures. One should facilitate constantly the elimination of débris. Thus, vaginal douches are given regularly in cases of a voluminous and discharging cancer of the cervix uteri; in cancer of the rectum, the diseased part should be extirpated subsequently and daily lavages should be administered through an artificial anus.

In a similar way, in cancer of the breast post-irradiative extirpation of the tumor has proven beneficial. Beside furnishing the histologic information for our statistics, this operation provides a great relief to the organism, in sparing it the necessity of riddance of bulky débris.

Our statistics show that the process of regression is influenced favorably by good after-care. Years ago, we reported statistically on two equivalent groups of cancer of the cervix uteri treated by roentgen rays. The first group comprised women who, after irradiation, had to return to their work in poor and even miserable home conditions, when they had just started to recover; the second group dealt with women who could afford a long stay at the clinic or at a sanatorium. Permanent five-year cures in the second group were almost twice as frequent as in the first one. This result proves clearly the great influence of systemic after-care in cancer therapy.

Thus, experience has taught us that the systemic treatment of the organism should not be neglected in radiotherapy of cancer; it greatly contributes to a permanent cure. But, on the other hand, it should not be over-rated, for without correct application of roentgen rays success cannot be expected. All those non-surgical and non-irradiative methods of cancer treatment propagated these last years have proven to be absolute failures. However, it is true that the results of roentgen therapy are convincing only in carcinomas of certain location, especially in cancer of the uterus and of the breast. In many other types of cancer, the results are so unsatisfactory that cures can be considered only as occasional chance results. But in spite of this, I claim that there are no refractory types of cancer. These last ten years have shown that many a so-called refractory form of cancer responded very well to an improved technic in irradiation. There are differences in radiosensitivity of the various cancer types. However, these quantitative differences could be established only after the dogma of refractory cancer had been relinquished. Good biologic studies on the reaction of the individual cancer types to roentgen radiation, and investigations concerning the collaboration of the organism in the healing of the defect caused by radionecrosis of cancer are based on the fact that cancer cells perish after application of a certain dose of rays. In case this anticipated reaction does not occur, one should not accuse mysterious biologic factors, but rather search for the cause of this misfortune.

Undoubtedly, it means increased responsibility to hold forth the conviction that our errors are responsible for failures, and not the roentgen rays *per se.*

I should like to add a few words about radiation injuries. Thanks to a well-developed dosimetric system, the period of severe injuries, especially of so-called burns of the skin, is past. But, as in cancer therapy, the skin must be loaded with rays to the limit of its tolerance, and it is necessary to know the mode of reaction of the skin in order to be able to avoid injuries.

The acute injury, the "burn," is caused by over-dosage. Aside from this, latent damage is always inflicted which is not manifested by a destruction of the skin or

of other tissues, but which produces a change in the sense of creation of a *locus minoris resistentiæ*. Coincidental, otherwise harmless injury may vulnerate such weakened tissue severely. In general, we assume, that the skin tolerates a dose of 100 per cent of the "skin unit." From eight to ten days after irradiation reddening shows and from four to six weeks later, tanning, the consistency of the skin undergoing no change. But if such a radiated skin is treated with heat or if 100 per cent of the "skin unit" is applied three times at intervals of six weeks between the applications, a condition of the skin occurs which we call "induration." The skin becomes thick like leather; it looks as if some liquid had been injected under high pressure. Such tissues then have become defenseless, and if, for instance, infection befalls them, necrosis ensues.

Induration is caused by injury of the vascular system. The intima of the blood and lymph vessels is very radiosensitive. Therefore, any tissue which has been irradiated with a dose near the limit of tolerance, carries a latent insult. We also speak of lesions caused by combination or summation of factors, meaning that exogene or endogene noxa of some or other type may coincide with a latent roentgen injury. The late roentgen lesions mentioned in the literature, which become manifest long after irradiation without any evident cause, are nearly always brought about by summation. But an efficient prophylaxis may be practised in order to avoid such lesions. The patient should be told that the radiated parts of the skin as well as of the underlying tissue, are more sensitive and less resistant than normal ones. A well-organized after-care should attend to the radiated region and avoid the coincidence of some other noxa.

Great experience and comprehensive knowledge are necessary in order to avoid mistakes and errors. Close collaboration with surgery and the other branches of medicine is of importance. Results will be satisfactory only if roentgen therapy is practised as a humane and courageous "art," cherished affectionately, studied diligently, and executed deliberately to its final consequences; never if resorted to merely as a last but hopeless effort in an ill conceived and timidly performed experiment.

GIANT-CELL TUMORS OF THE SPINE

WITH REPORTS OF THREE CASES[1]

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THIS interesting tumor has been known for many years under a wide variety of names. Nelaton (12), in 1860, was apparently the first to recognize its benign character and to separate it from malignant bone tumors under the caption of "tumeur a myeloplaxes." There has been and still is some contention that this is not a tumor at all but merely bone reaction to hemorrhage, so we find it referred to by Bloodgood and others as "hemorrhagic osteomyelitis." For many years the benign character of the lesion was opposed by many observers and the presence of a malignant variety is still maintained by many outstanding men. We find the condition referred to in the older British literature as "myeloid sarcoma" or "myeloma," and in the American literature as "giant-cell sarcoma." The work of the original Bone Registry Committee of the American College of Surgeons brought order out of this confusing multiplicity of names and ideas by establishing the fact that it is a clinical entity, neoplastic in origin and benign in nature. Their terminology of benign giant-cell tumor is now almost universally accepted.

This condition is relatively uncommon, occurring probably half as frequently as primary malignant bone tumors. It has a rather characteristic age incidence, the majority of the cases occurring in the latter half of the second and the third and fourth decades. The sexes are about equally affected, though some observers find it to be slightly more common in women than in men. The sites of involvement, in their order of frequency, are: lower end of femur, upper end of tibia, lower end of radius, the epiphyses of other long bones, the jaws, and the spine. Kolodny (9), in his analysis of the Bone Registry material in 1927, found the spine to be the seat of the lesion in 8 per cent of cases of benign giant-cell tumor.

The radiological findings in the majority of cases of this disease are striking and characteristic. The lesion practically always involves the epiphysis of the bone, is central in origin and expansile in type, and is frequently asymmetrical, one condyle only of a bone being involved. Cortical destruction and expansion of periosteum, with subperiosteal new bone formation, produces a "blown out" appearance. The line of demarcation between the tumor and normal bone is usually sharp and clean-cut and may be marked by a thin shell or rim of condensed bone. Coarse, bony trabeculæ throughout the tumor give it the characteristic loculated appearance in the radiographs.

As well as this group which produces this characteristic appearance, there occurs another group, less numerous, which presents none of these radiological findings, yet which, on surgical exploration and on microscopic examination, are typical benign giant-cell tumors. Isolated reports of this type of case have appeared in the literature, and Kirklin and Moore (8), in an analysis of benign giant-cell tumors seen at the Mayo Clinic, found 50 per cent of their cases to be of this character. They gave it the name of "lysis" type of benign giant-cell tumor. These lesions are frankly osteolytic with no attempt at bone repair. The cortex is usually completely absorbed and the demarcation between tumor and normal bone is not very sharp and no trabeculation is present. These

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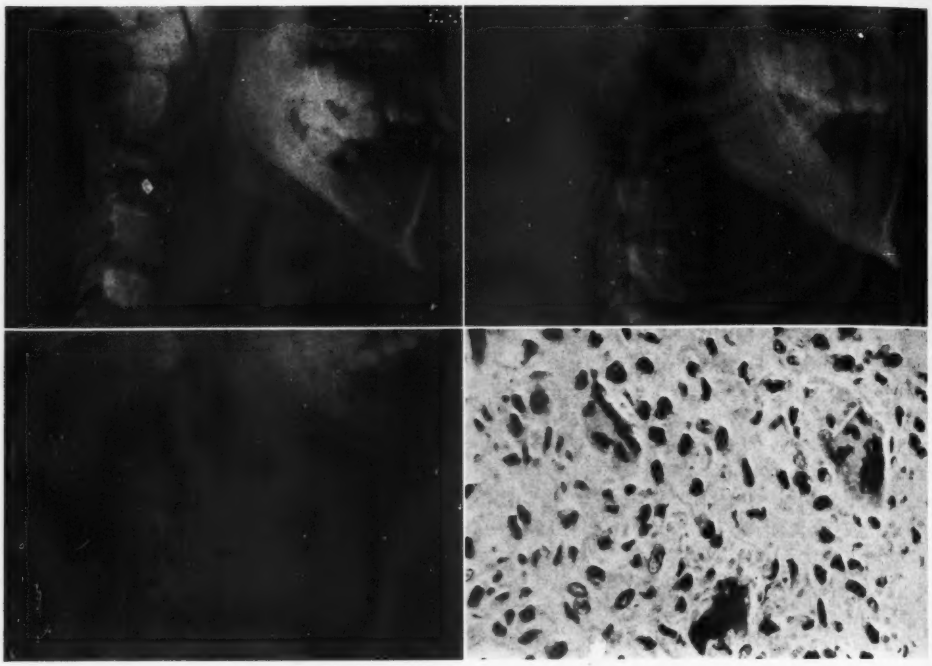

Fig. 1 (*upper left*). Case 1, Mr. A. M., Oct. 22, 1931. Film shows benign giant-cell tumor of the third cervical body with pathological fracture. Note characteristic multi-loculated appearance of the tumor.
Fig. 2 (*upper right*). Case 1, Nov. 19, 1931. Film shows benign giant-cell tumor of the third cervical body. Note marked absorption of bone in the third cervical body with collapse and kyphosis at this point. No radiation treatment had been given prior to this date.
Fig. 3 (*lower left*). Case 1, Jan. 22, 1932. Six months after radiation treatment by means of high voltage x-ray. The bone absorption and the kyphus are still present. The patient is symptom-free.
Fig. 4 (*lower right*). Case 1, Photomicrograph of benign giant-cell tumor of the third cervical body.

findings are frequently found associated with a short clinical history, so that these are probably more rapidly growing tumors which do not allow time for the typical reactive bone changes to take place. Such a case is usually mistaken for one of the primary malignant newgrowths of bone or for secondary tumor, to which there is close resemblance.

Cartilage, either epiphyseal or articular, seems to offer definite resistance to the disease process, whether it be the ordinary or the lytic type; consequently, the process is usually limited to the epiphysis if the epiphyseal line is not fused and extension to adjoining joints is an uncommon and late complication. Pathological fracture is relatively common, particularly in weight-bearing bones, and may be the first indication of disease.

Allowing for differences in anatomical structure, benign giant-cell tumors in the spine present the same characteristics. The disease may arise in any part of a vertebra and extend to adjoining other parts by direct continuity. There seems to be a special tendency for pedicles and transverse processes to be involved. The cartilage of the intervertebral disc is usually intact, even though the whole vertebral body may be involved. Both types of tumor, described above, may occur in the spine and in both types diagnostic difficulties are definitely increased due to the multiplicity of bone lesions which commonly affect this structure. The relative infrequency of this tumor in the vertebral column and the difficulties attending its correct diagnosis have prompted us to report the following three cases.

Fig. 5 (*left*). Case 2, Miss A. M. S., Oct. 22, 1936. Film shows benign giant-cell tumor of the first lumbar body, "lysis" type. Note destruction of lateral aspect of body of first lumbar vertebra and destruction of pedicle and lamina of transverse process.
Fig. 6 (*center*). Case 2, Oct. 22, 1936. Lateral view of same case shows involvement of posterior half of vertebral body, pedicle, and lamina.
Fig. 7 (*right*). Case 2, Photomicrograph, × 200, from biopsy removed Oct. 28, 1936.

Case 1. The surgical and pathological aspects of this case have been previously reported by MacFarlane and Linell (10). The patient, A. M., a white male 35 years of age, was admitted to the Emergency Department of the Toronto General Hospital on Oct. 22, 1931, and gave the following history. In the evening prior to admission, while attempting to crank his car, the engine back-fired. He felt something "snap" in his neck and had pain in the neck and back of his head, associated with limitation of movement. There had been no symptoms prior to the injury.

Radiological examination revealed a compression fracture of the third cervical body, associated with definite pathological changes in this vertebra. Normal bone striation was replaced by a coarse, loculated trabeculation, giving a definite multicystic appearance. The cortex was intact, apart from the area of fracture, but anteriorly the cortex of the body bulged forward and the posterior cortex protruded slightly backward. The total bone density of this vertebral body was definitely decreased (Fig. 1). The character of the lesion led to a radiological diagnosis of benign giant-cell tumor of the third cervical body. Thorough clinical and radiological investigation failed to reveal any evidence of other bone disease or of a primary carcinoma. A further radiological examination made on Nov. 19, 1931, four weeks after his injury, showed absorption of the upper three-fourths of the third cervical body with formation of a definite kyphosis (Fig. 2).

Two weeks after this x-ray examination, radiation therapy by high voltage x-ray was commenced. The patient received 600 r measured on the skin to each of three portals, centering on the third cervical body. He was discharged from the hospital finally on March 9, 1932, at which time his third cervical body was completely absorbed, except for a fringe of its inferior cortex (Fig. 3). At this time he was wearing a light support and was free of any clinical symptoms. Some three months later, after returning to work, he was thrown from a truck and sustained a fractured skull from which he died. Autopsy proved the lesion in the third cervical vertebra to be benign giant-cell tumor. It also proved the cause of death to be his fractured skull and not compression of the spinal cord at the site of his tumor. Microscopic section from the third cervical body shows benign giant-cell tumor (Fig. 4).

Comment.—The marked lysis of bone in this case occurred before radiation therapy was commenced. Similar bone absorption

and apparent extension of disease frequently occurs shortly after institution of radiation therapy to these tumors, to be followed later by bone regeneration. Treatment was effective in causing regression of the tumor and we feel, would have controlled unquestionably his disease if he had not unfortunately died of fractured skull.

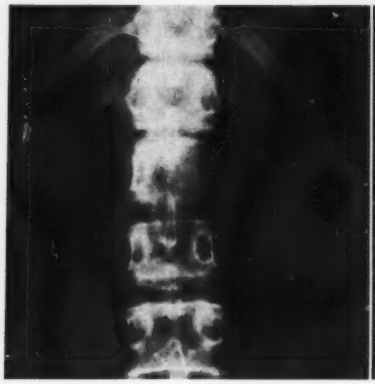

Fig. 8. Case 2, Jan. 18, 1937. Benign giant-cell tumor, "lysis" type, of first lumbar body. This film was made ten weeks after surgical exploration and biopsy and interstitial radium therapy. Note bone regeneration in vertebral body and from periosteum of transverse process.

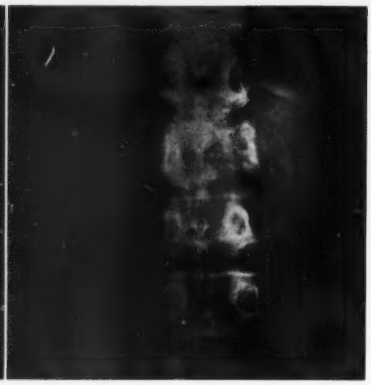

Fig. 9. Case 2, April 5, 1937. This film was made ten weeks after first series of high voltage x-ray therapy and three months after interstitial radium therapy. Note continued and marked bone regeneration in the vertebral body and transverse process.

Case 2. A. M. S., a white female 13 years of age, was referred to our office on Oct. 22, 1936, for radiological examination of her lumbar spine. Her story was that while swimming, two months previously, she had slipped on a raft and "strained her back." Her back was somewhat "stiff" for a few days, then all symptoms disappeared to return after an interval of two or three weeks. For the past month she had had more or less constant ache in her back which had increased up to the time of her examination.

Radiographs of her lumbar spine showed a destructive lesion involving the left lateral and posterior aspects of the first lumbar body, the entire left pedicle and transverse process, and the major portion of the lamina on the left side. The lesion was entirely osteolytic in nature, cortex and cancellous bone both being destroyed without any reactive bone changes in the vertebral body, nor any periosteal reaction. No trabeculation was present within the lesion and the line of demarcation between the lesion and normal bone was very indistinct. The intervertebral disks above and below the involved body were intact. There was no evidence of fracture, nor any evidence of an associated soft tissue mass (Figs. 5 and 6). We felt that the findings were unquestionably those of primary tumor of bone but could not be certain as to its type.

On Oct. 28, 1936, the lesion was explored by Dr. R. R. Graham who removed a portion of the tumor for biopsy. Microscopic examination of the tissue by quick section showed it to be a typical benign giant-cell tumor (Fig. 7). At the time of the operation twenty 2-mg. radium element needles with filtration of 0.5 mm. of platinum were embedded by one of us (G. E. R.) in the tumor for a total dose of 4,800 milligram-hours. Films made ten weeks later, on Jan. 18, 1937, (Fig. 8), showed beginning bone regeneration in the vertebral body and lateral to the body in the region of the transverse process. At this time the patient was free of pain. A

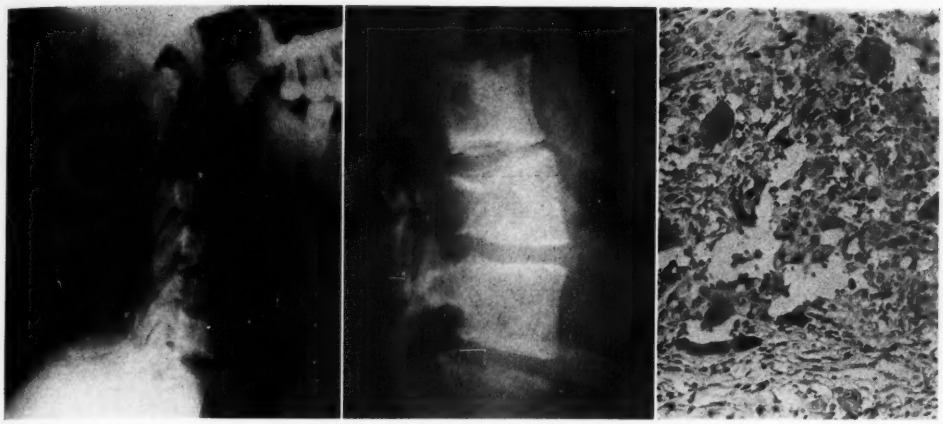

Fig. 10 (*left*). Case 3, Miss Des L., Aug. 4, 1934. Malignant giant-cell tumor of entire fifth cervical vertebra and of the body of the second cervical vertebra. Note irregular cancellous and cortical destruction.
Fig. 11 (*center*). Case 3, Aug. 4, 1934. Malignant giant-cell tumor of the second, third, fourth, and fifth lumbar vertebræ, with pathological fractures of the third and fifth bodies.
Fig. 12 (*right*). Case 3, Photomicrograph of Case 3, × 200. This was reported pathologically as giant-cell tumor (xanthosarcoma).

series of high voltage x-ray treatments was carried out, giving 1,200 r over each of three portals centering on the first lumbar body. Subsequent films made ten weeks later, April 5 (Fig. 9), showed a very marked degree of bone regeneration throughout the tumor. At this time the patient had full range of painless movement in her back and was allowed up out of bed.

Comment.—This case presents a number of interesting features, as well as its unusual radiographic appearance. The patient's age of 13 years is well below the average for this tumor. The absence of increased bone absorption and the very prompt response to treatment in the form of bone production are unusual and encouraging, and the patient should go on to complete regeneration of bone.

Case 3. C. D. L., a white female, 28 years of age, was admitted to the Ontario Institute of Radiotherapy, Toronto General Hospital, on Aug. 3, 1934. She gave a history of pain and weakness in her back for two years and soreness in her chest, neck, left arm, and pelvis for six months. During the six months prior to admission she had lost 27 pounds in weight.

Physical examination revealed tenderness over the cervical, mid-thoracic, and lumbar spine with painful limitation of movement, a palpable mass in the region of the posterior superior spine of the ilium and a mass of glands in the left side of her neck.

Radiological examination of the cervical spine showed pathological changes involving the entire fifth cervical vertebra. The changes consisted in irregular, globular areas of bone destruction, cortical and medullary, throughout this vertebral body and extending backward to involve pedicles, laminæ, and spinous process. The picture was complicated by the presence of pathological fracture. There was no involvement of the intervertebral disks above or below the fifth cervical vertebra. The second cervical vertebra showed a rather large single area of bone destruction, involving the anterior part of the body and extending upward into the odontoid process (Fig. 10). Films of the remainder of this patient's skeleton showed similar destructive changes in the eighth, ninth, eleventh, and twelfth thoracic vertebral bodies, in numerous ribs, in the third, fourth, and fifth lumbar vertebræ, in both ossa innominata and the sacrum. Pathological

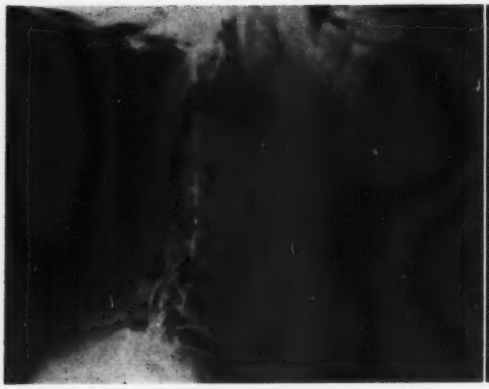

Fig. 13. Mr. C. P., May 23, 1934. Hemangioma of the sixth cervical body which closely simulates benign giant-cell tumor.

Fig. 14. Miss I. S., April 20, 1934. Ewing's sarcoma of the fifth cervical body with pathological fracture and paraplegia. Note close resemblance between this illustration and Figure 1, Case 1. In this case the diagnosis of Ewing's sarcoma was not considered until microscopic examination was done.

fractures were present in the lesions in the third and fifth lumbar bodies (Fig. 11). There was no evidence of disease in either lung. The character and multiplicity of the lesions in bone and the absence of lung involvement in a woman of 28 years of age presented a nice problem in diagnosis. We felt that the differential diagnosis lay between secondary carcinoma and myeloma, with the weight of evidence in favor of carcinoma in spite of the absence of lung metastasis.

Microscopic examination of tissue removed for biopsy led to the pathological diagnosis of giant-cell tumor (xanthosarcoma) (Fig. 2).

Comment.—This case may be used to illustrate the discrepancy which is occasionally seen between clinical and radiological findings on the one hand and the microscopic findings on the other. There will be some who will argue that this case is not giant-cell tumor at all, and others will accept it as representing that group of tumors which may be termed "malignant giant-cell tumors" or "giant-cell sarcomas." Certainly these cases are vastly different from benign giant-cell tumors clinically and in their radiological findings, and must be considered as a separate group for purposes of treatment and prognosis.

DIFFERENTIAL DIAGNOSIS

Benign giant-cell tumors, when situated in their usual location in the epiphysis of a long bone and presenting the characteristic radiological findings discussed above, do not usually offer much difficulty in diagnosis. However, even in long bones and particularly in the spine, their x-ray picture may be closely simulated by a number of other lesions of bone. Hemangioma of a vertebral body, while usually producing perpendicular striations without cortical expansion, may at times present globular loculation, suggesting benign tumor (Fig. 13). We have observed Ewing's sarcoma of the fifth cervical body to resemble benign giant-cell tumor so closely that the correct diagnosis was established only by microscopic examination of tissues removed at laminectomy, done in the hope of relieving paraplegia (Fig. 14). Even secondary carcinoma of the spine may closely approach the characteristic appearance of giant-cell tumor, and if one vertebral body only is involved the differentiation may be very difficult.

Even greater difficulty in differential diagnosis is presented by those cases which do not present the usual radiological findings—the so-called lysis type of giant-cell-tumor in which the lesion is purely de-

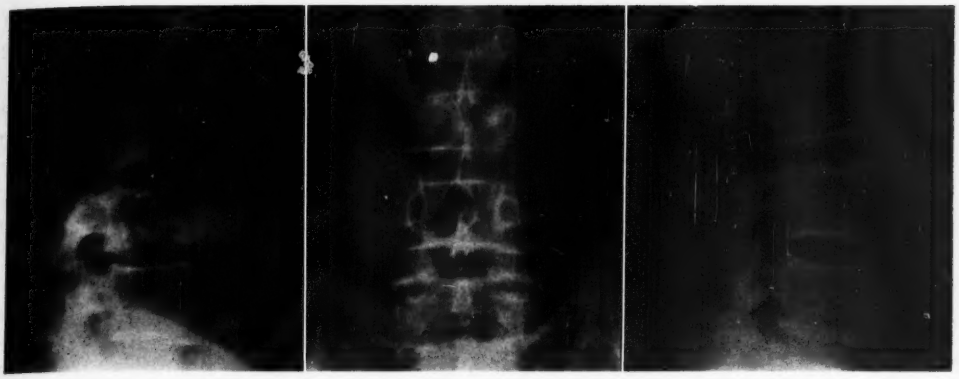

Fig. 15 (*left*). Mrs. E. M., May 31, 1934. Hodgkin's disease of the first, second, and third lumbar bodies with pathological fracture in the third.
Fig. 16 (*center*). Mrs. J. L., Jan. 30, 1936. Neurofibroma of soft tissues, producing rounded bone defects in the third and fourth lumbar vertebræ on the right side. The bone defects are clean-cut, with sharp demarcation between the area of destruction and normal bone.
Fig. 17 (*right*). Lateral view of patient shown in Figure 16.

structive with no apparent attempt at bone repair. The age of the patient may be of help in differentiating these cases as it is unusual to have malignant osteolytic tumors in young people, though the majority of these cases will require microscopic examination of tissue to allow of a positive diagnosis.

Primary malignant tumors of bone and metastatic tumors are, of course, the most frequent sources of error in this group though rarer lesions occasionally enter into the differential diagnosis. Hodgkin's disease of bone may rarely involve a single vertebral body and present a radiographic picture similar to these lytic tumors (Fig. 15). Occasionally pressure from an overlying soft tissue tumor produces a crescentic bone defect with rather indefinite outlines which may be confused with primary tumor of bone, as in one of our recent cases (Fig. 16). Here the bone defect was due to an encapsulated neurofibroma, lying immediately adjacent to the vertebral body

DISCUSSION

The question of malignant variants of giant-cell tumor of bone has been widely discussed and pathologists are divided in opinion in this regard. Theoretically, malignant giant-cell tumor might occur in either one of two ways: first, as a primary tumor malignant from its inception, and second, as a metaplasia from a simple benign giant-cell tumor. That either of these processes occur is refuted by Geschickter and Copeland (4), who maintain that the cases of so-called giant-cell tumor which metastasize are in reality not giant-cell tumors at all, but osteogenic sarcomas containing numerous tumor giant cells. With regard to metaplasia of a benign giant-cell tumor to an osteogenic sarcoma they point out that a benign giant-cell tumor recurring after curettage and with super-added infection may present a microscopic appearance which is indistinguishable from osteogenic sarcoma, yet which is still benign and does not metastasize.

Contrary to this is the frequently quoted case reported by Ewing and Stone (3), in which a typical benign giant-cell tumor recurred after curettage and, following radiation treatment and infection, underwent malignant degeneration and killed the patient by metastasis. Cases of malignant giant-cell tumor have also been reported by Coley (1), Peirce (14), Thurstan Holland (7), and others, so that, for purposes of treatment, we feel we must bear in mind that malignant tumors of this type

do occur. For practical purposes, whether they are microscopically malignant giant-cell tumors or osteogenic sarcomas is of less moment, as the response to treatment and the prognosis remain the same. In many of these questionable cases there are unusual features, in the clinical history, the location of the lesion, or the age of the patient, to mark them from the onset as unusual.

One cannot discuss the radiological findings of any group of bone tumors without considering also the value and advisability of doing biopsies. A careful clinical history, taken in conjunction with a thorough and competent radiological investigation, will differentiate benign from malignant bone tumors in at least 80 per cent of cases. In certain of the remaining cases the pathologists also may have great difficulty in deciding this point, as a great many of the cases in which clinical and radiological examinations fail are problem cases, being atypical and unusual. The taking of biopsies in cases of bone tumors has been opposed by a number of pathologists, notably Ewing (2), because of the dangers of infection and the feeling that dividing the natural barriers, notably periosteum and cortical shell, leads to earlier local extension and generalized dissemination of the disease. The danger of infection has been definitely lessened by improvement of surgical technic in bone cases, but its possible occurrence must always remain. Aspiration biopsy, as evolved by Martin and Ellis (11), probably reduces the dangers of biopsy, both real and theoretical, to a minimum, and this method should prove to be very satisfactory in giant-cell tumors in which the cortical shell is thin.

In tumors of the spine in which surgical excision is impossible, the practical value of biopsies is much less as conservative methods of treatment must be employed, regardless of the type of tumor present.

The treatment of giant-cell tumor of bone has shown progressive improvement with changing conceptions of the pathology of this lesion. For many years, before the benign nature of the tumor was realized, amputation was the universal method of treatment and unquestionably this fact contributed, to a considerable extent, to the earlier statistics of cures in cases of bone sarcomas. Later, local resection of the lesion was done and this was followed by the operation of curettage. Later still, in an effort to prevent recurrence following curettage, the cavity was swabbed out with an escharotic—either zinc sulphate or carbolic acid followed by alcohol. This method has given good results in the majority of cases but is not without definite drawbacks in the possibility of hemorrhage and infection and the certainty of recurrence in a considerable number of cases. Geschickter and Copeland (4) report 31 recurrences after a single curettage in a series of 222 cases, or 14 per cent, while Kolodny (9) states that recurrence takes place in approximately 20 per cent of cases following single curettage.

Since Pfahler (13), in 1906, first treated a case of benign giant-cell tumor of bone by x-ray, radiation therapy has been slowly gaining ground and has been given great impetus by the excellent work of Herendeen (5,6), Pfahler and Parry (13), Peirce (15), and others. The response of these tumors is usually slow and is frequently preceded by a stage of lysis and apparent extension of the disease, to be followed by bone regeneration and repair.

While controversy may continue as to the relative merits of surgical and radiation treatment of benign giant-cell tumors of long bones, there can be little question that radiation must be the method of choice when the disease affects the spine. Cases 1 and 2, here reported, both show clearly the value of radiation therapy in this condition, though the patient reported as Case 1 died before the treatment could be followed through to conclusion and the patient reported as Case 2 has been under treatment for too short an interval to allow of anything but a preliminary report. Her progress so far has been very encouraging and a good final result is almost certain.

CONCLUSIONS

1. Two types of benign giant-cell tumor of the spine are described and some of the difficulties of radiological diagnosis in each type are discussed.

2. Two microscopically proven cases of benign giant-cell tumor of the spine, illustrating these different types of tumor, are reported.

3. The value of radiation treatment in benign giant-cell tumors of the spine is indicated.

4. One case of malignant giant-cell tumor of the spine is also reported.

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THE TREND IN RADIOTHERAPY OF CANCER

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THE biological effects of radium and x-rays were discovered by the production of accidental injuries. Marie Curie's hands never recovered from their damaged condition, the result of contact with the radium she was isolating, though it was Becquerel's historic burn that drew direct attention to the destructive capacities of this agent. The lesions from x-rays of the early patients and operators are well known, but x-ray cancer of the operator became a thing of the past with the introduction of the hot cathode x-ray tube, the output of which can be controlled at a distance. Patients may still have x-ray cancers as a result of treatment, but there will be no more martyrs among operators.

The therapeutic value of radiation came later. The chief advance in the use of radium in the early days was the introduction by Dominici of the principle of heavy filtration, but the extraordinary time-lag which is observed between scientific discoveries and their practical application prevented for more than ten years an intelligent use of the facts pointed out by Dominici. The development of the use of x-rays was likewise hampered for a longer period by a lack of application of the available experimental knowledge. Regaud and his co-workers had begun a series of studies on the effects of radiation on cells, but the most important contribution in which biological methods were used to study the effects of radiation is the monograph by Krönig and Friedrich, published in 1918. They carried on an enormous series of very intelligent experiments, but, owing to the difficulties in measurement of both the radium and x-ray intensity and the lack of suitable biological material, missed a number of important facts. For example, they found that filtered gamma rays were four times more effective than an equal amount of x-radiation, but they noted the important fact that a far deeper skin erythema followed the application of a single dose of filtered roentgen rays than when one-tenth of the same dose was given on ten successive days, thus laying the foundation for divided-dose therapy. This passed more or less unnoticed and the tendency was to follow the dictum of Seitz and Wintz, and attempt to apply a single sterilizing dose to the tumor, which was computed at approximately 130 per cent of an erythema.

The firm basis for the application of this principle was laid down by Regaud (in a series of papers from 1906 to 1922), who showed that sterilization of the testicle in animals was followed by less damage to the skin when the treatments were divided into three or four successive applications. Regaud called attention to the rhythmic appearance of mitoses in tissues and pointed out that in the testicle a continuous feeble dose of radium might cause complete sterilization of a tissue by killing the mitotic cells only. This introduced the principle of avoiding damage to the healthy tissues but at the same time destroying the neoplasm. Under Regaud's direction Coutard developed a practical technic for the treatment of human cancer and laid the foundation for the modern effective use of radiation.

At the same time Wood, Prime, and Packard were beginning their demonstration of the independence of the biological effect in relation to the wave length of the radiation used when applied in a single dose to suitable biological material. This was confirmed and amplified by Holthusen and his school in regard to the erythema dose on the skin.

Nevertheless while these facts have been available in print from 1922 on, they still have not penetrated into the general field of practical therapy, and old-fashioned methods are still used by the majority of radiotherapists. To Regaud is due the stress laid upon the rate of giving of radiation both with x-rays and gamma rays and he and his co-workers formally established the fact that better results are obtained by prolonging the dose with either type of radiation over a considerable period, though the exact details for the individual patient still escape a definite formulation. In other words, the treatment must be adapted to the individual and no dogmatic and general rules are as yet possible.

However, the collection and publication of a large amount of clinical material is beginning to show, as Coutard has repeatedly said, that rapidly growing tumors should be treated somewhat more intensively than the slow-growing, presumably dependent upon the fact, as pointed out by Bergonié and Tribondeau, that mitotic cells are more sensitive than resting cells and in slow-growing tumors the period of radiation must be extended considerably as the mitoses are infrequent and few, and the tissues of the tumor must be kept nourished, so to speak, to preserve all the normal structures in order to obtain permanent results. Too rapid and too intense dosage shuts off the blood supply from the tumor and quickly renders the normal tissues so sensitive to radiation that doses destructive for the tumor cells soon become impossible.

From careful studies of the rate of administering radiation made by Coutard and by Holthusen and his collaborators on human material, the absolute necessity for a low rate of giving of x-rays is now generally acknowledged, though practically still but little used. Thus we see in a recent number of RADIOLOGY the statement by an experienced clinician that equally good results are obtainable by giving x-rays at the rate of 15 or 20 r per minute or even higher as are obtained with a slower rate of 3 or 4 r per minute, though this was demonstrated as untrue by Regaud and Holthusen. Eight years have elapsed since proof of this fact and still it has not penetrated into practical therapy. An obvious hindrance to practical application is the length of time required to make the exposures and, hence, diminution of the number of patients who can be treated.

This statement applies only where an attempt is being made to produce a permanent cure, which implies the destruction of all living cancer cells. In cases in which simple palliation is the only result that can be expected, the radiation can be given more rapidly, provided it is properly spaced in time.

Another hindrance to the use of the Coutard method has been the insistence of the author on the fact that serious lesions of the skin and mucous membranes are essential for the production of a cure. It is still being held by many courts that a skin lesion from radiation is an evidence of malpractice, a position as antediluvian as to assume that the scar of an abdominal incision carried the same legal liability. But the necessity for serious lesions is not true in all instances, as cures can often be obtained without them if the administration of the radiation is sufficiently slow, the spacing properly judged, and the skin not hypersensitive. For there are patients with skins so sensitive that 3,500 r, given at a rate of 4 r per minute and only 200 r applied daily, will result in such a severe injury that the treatment has to be abandoned. However, this situation can be obviated provided radiation at higher voltages is available and the same patient whose skin was damaged by a dose of 3,500 r at 200 kv., is able to receive 8,000 r at 4 r per minute and 200 r per day when the voltage is 800 kv.

This raises the question of the value of the higher voltages. The reason why radium has been considered so much more effective than x-ray has been due to two facts: that the average 4-gram pack at 10 cm. does not give a rate higher than some 4 to 5 r per minute on the skin and, secondly, that gamma radiation is equivalent to a voltage of about 2,000,000. With such

short wave lengths, even though the depth dose is much less than with x-ray, extraordinarily good results have been produced, but entirely without any appreciation of the scientific basis of this difference, which lies wholly in the fact that the back scatter from the tissues to the skin with gamma radiation is of the order of 5 per cent of the impinging dose, and this is also true of 800 kv. x-rays. With 200 kv. x-rays the back-scatter from the tissues to the skin is 45 per cent of the impinging dose. Thus in giving 200 r with 800 kv. or with radium, only some 210 r units reach the skin, while with 200 kv. a similar dose means approximately 290 r units in the skin.

This is the chief advantage of the use of the higher voltages of x-rays and at 800 to 1,000 kv. the clinical results are apparently perfectly equivalent to those of radium. There is the additional advantage that, owing to the approximately parallel beam obtained by the use of a long skin-focus distance of from 100 to 150 cm., such as is possible with the higher voltages of x-rays, the depth dose at 10 cm. with moderate portals may be 50 or 60 per cent of the impinging radiation, whereas with the radium pack it is not more than 25 per cent of the impinging dose measured in air.

In cases in which many portals can be used these facts are not so vital for effective therapy because under these circumstances no excessive skin dose has to be given over any individual portal, but when the portals are limited, as in the treatment of cancer of the upper respiratory and oral tracts, the advantage is so considerable that it may determine the possibility of a cure which may not exist at the lower voltage radiations. Nevertheless the author has, by a careful study of the patient's condition, been able to cure a carcinoma of the larynx with 150 kv. radiation by proper extension of the time of radiation and the use of small quantities, not over 3 to 4 r per minute, and a total of from 150 to 200 r per day. The reason for this is, of course, that the amount of penetration required is small in this site.

The sole advantage that radium possesses at present over the higher voltage x-rays lies in the possibility of the insertion of highly filtered radiation into the substance of the tumor at the same time that heavy x-ray radiation may be applied through the skin. This condition does not exist in connection with a carcinoma of the larynx, hence the tendency to abandon radium for its treatment. Apparently for this particular form of neoplasm x-rays will soon supplant surgical operation and will in many cases not only cure the patient but leave him in such shape that his ability to talk is not compromised. However, even in such a situation it is dangerous to generalize, and if the growth has already destroyed a considerable part of the vocal cord, complete restoration of the voice is obviously impossible.

This brings up the question of the limitations of radiocurability, which has recently been discussed in an excellent article by Lenz. In it he points out that notwithstanding all that has been learned in late years concerning the way in which radiation should be applied there are many conditions which interfere with effective treatment. Thus while it is possible to cure a carcinoma of the skin with ease, to the same type of tumor in the esophagus it is practically impossible to deliver an adequate dose, and even if effective radiation has been applied, the accident of perforation into the mediastinum—with the resulting infection—may cost the patient his life, although the radiation has destroyed the tumor. The existence of syphilis renders it almost impossible to apply a satisfactory amount of radiation to the tongue without causing extensive sloughing. In other words, the vessels which are damaged by the syphilis are also damaged by the x-ray or radium and the resulting blood supply may be quite insufficient. Also, bone necrosis is not infrequent in the jaw if heavy dosage is given, especially in those who have infected tooth-roots. The easy induction of pulmonary fibrosis in addition to the high radioresistance of lung cancer prevents any effective therapy in this region. Again, there are patients

whose susceptibility to the general effects of radiation is so great that they will refuse treatment. Curiously enough, the use of from 800 to 1,000 kv. x-rays with 10 × 10 cm. portals seems to give less x-ray sickness in dosages of 200 r than the corresponding 200 kv. radiation. Perhaps, as Stone has recently shown, this is because the scatter with the higher voltages is forward so that the prism of tissue irradiated is less in bulk than at the lower voltages where there is still a good deal of scatter out of the line of the direct beam. All these limiting factors have, up to the present time, prevented the effective treatment of any type of neoplasm, except of the skin, the cervix uteri, and certain oral and upper respiratory tract growths. For these, radiation is on an equal or better footing than surgery, as there are now a considerable number of five-year cures of carcinoma of the cervix by radiation though in an inoperable stage.

The trend of late years has been toward electrical engineering improvements in x-ray apparatus so that higher voltages are now at our disposal at a fairly moderate cost and these machines are to a certain extent replacing radium, as illustrated by the fall in the price of radium. But if radium were very cheap would it again return to its old popularity? This may seem a vain question, but the developments in experimental physics in the last year or two point to the possibility of the production of vast quantities of radio-active material by a relatively simple procedure, that of breaking up the atom of various substances by impacts with heavy hydrogen atoms. The machine which does this was invented by Professor Ernest O. Lawrence, of the University of California. He is now working with energies equivalent to about 6,000,000 volts and has produced approximately one kilo of radio-active sodium. It has a half-life of fifteen hours, hence is not particularly useful, though interesting experimentally as, in theory, it is possible to inject it into the body. But the injection of radio-active material into the veins has never proved effective in the treatment of cancer nor even of leukemia and presumably never will, because circulation in the resistant types of growth which at present cannot be treated with x-rays is slow, and most of such injected sodium would be exerting its energies in destroying the kidneys, liver, and bone marrow, and only a small quantity would reach the tumor. But the production of these radio-active elements is a matter primarily of energy and so far it has been possible to produce small quantities of radio-active bismuth and vanadium, which have a longer half-life. If energies equivalent to 20,000,000 volts can be produced with this machine, there is no theoretical reason why the long life radio-active substances cannot be made. We are, in other words, within striking distance of the production of radium by the radiation of uranium.

The one difficulty with large quantities of radium has always been the question of protection, but recent developments in pack construction, such as that shown at the Fifth International Congress of Radiology in Chicago, demonstrate that both the patient and the operator can be completely protected from the radiation during the placing of the patient and the radium automatically substituted while the operator is safely out of reach behind thick lead walls.

It may be that in the future there will be a swingback to the employment of large quantities of these synthetic radio-active materials if the skin-radium distance can be the same as the skin-focus distance with x-rays, so that again radium will replace x-rays in many fields, especially for the radiation of internal growths over long periods of time. Cyclotrons of great capacity will shortly be constructed and the attempt to activate the elements of higher atomic weight will no doubt be begun within a year, so that soon it will be definitely known whether this most dramatic adventure in modern physics offers anything practical in the attack on cancer.

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METHOD IN RADIOTHERAPY

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DURING recent years the tendency among therapeutic radiologists has been to emphasize penetration. This tendency has now reached such proportions that other important factors often receive little or no attention. Almost everywhere there has been an increasing demand for more and more penetrating rays, and satisfaction of this demand has been sought in higher and higher potentials. In many parts of the country apparatus designed to generate roentgen rays at potentials from 600,000 to 1,000,000 volts, or even higher, has been installed and is being used to treat a variety of tumors. In a few institutions apparatus of this kind has been in use for five or more years, but in most places the installation of such equipment has been more recent.

Several factors have stimulated this desire for more penetrating rays. For many years radiologists had observed that while some malignant neoplasms, notably the epitheliomas of the skin, could be cured or greatly influenced by exposure to strong doses of rays generated at moderate or even at relatively low potentials (140 kilovolts or even 100 kilovolts), tumors derived from epithelial or connective tissue cells and situated in the depths of the pelvis, abdomen, or thorax, or in other regions, were influenced much less or not at all by the same doses or even by still larger doses of rays. No doubt, an important reason for this difference was that, with roentgen rays generated at potentials below 150 kilovolts, a considerable proportion of the beam of rays was made up of comparatively long wave lengths, and these were absorbed largely by the layers of tissue at or near the surface of the body. The beam necessarily contained a certain proportion of rays of shorter wave length, but the proportion of such rays was relatively small—too small to have a pronounced or lasting effect on deep and resistant tumors. With a beam of rays generated at 140 kilovolts and filtered through 4 mm. of aluminium, and with the target of the tube at a distance of 12 inches (30.5 cm.) from the skin, the proportion of the surface dose reaching a depth of 10 cm. was only about 18 or 20 per cent. Even with a beam of rays generated at 200 kv. and filtered through 1 mm. of copper, the proportion of the surface dose reaching a depth of 10 cm. does not exceed 35 per cent. Nevertheless, even this moderate difference yielded noticeably superior results in the treatment of certain kinds of tumors deep beneath the surface of the body.

A second reason for the trend toward higher potentials has been the desire to avoid the deleterious changes in the skin often observed after strong doses of roentgen rays of relatively long average wave length. There is no doubt that, in this respect, the shorter the average wave length of the beam of rays the smaller is the effect on the skin and subcutaneous tissues because these tissues absorb a comparatively smaller proportion of the surface dose. Hence, larger surface and depth doses can be given with less likelihood of injury to the skin.

A third reason relates to the so-called selective action of roentgen rays of short wave length. This doctrine, formulated and promulgated by Regaud, was based on the point already mentioned that, when a beam of rays is directed to any part of the body, the shorter the effective wave length of the beam the smaller the proportion absorbed by the skin and subcutaneous tissues. Hence, the cells of the deeper tissues receive a correspondingly larger dose and are influenced that much more, or the same effect on deep tissues can be produced with a smaller dose—a quantitative dose insufficient to cause an inflammatory reaction in the skin. However, to ascribe to the rays the power of selective effect on cells is mis-

leading. It is not the rays that select certain kinds of cells on which to exert their action. The only discrimination exercised by the rays is that of variation in penetrating power according to wave length. The word "selection" implies a conscious or active property. As a matter of fact, the only selection that enters into the action of roentgen rays on cells is the great variation in susceptibility of different species of cells. Any selective property, therefore, belongs to the cells themselves, but this is a purely passive and not an active property or quality.

As the trend toward higher and higher potentials has developed, the emphasis on penetration has become so great that other important factors are overlooked entirely or do not receive the degree of attention which they deserve. I refer particularly to the factor of absorption and to another factor which will be mentioned presently.

In this country the large amount of publicity given to technical and scientific developments in general, and to high voltage generators of roentgen rays in particular, has misled non-specialized physicians and the public into believing that the secret of curing cancer lies in the use of rays generated at higher and higher potentials, and that the higher the voltage at which an "x-ray machine" is capable of operating, the better *must be* the results. In fact, this public impression has become so widespread that patients often ask the radiologist what is the strength of his machine. Sometimes this impression has arisen from the unwise statement of a radiologic competitor that "Dr.—'s machine is not strong enough." Of course, few patients know anything about the subject, except what they may have read in news items or health columns of newspapers or in magazine articles. Owing to the great industrial development in this country and to a general glorification of science, the average person, whether physician or layman, has become a worshipper of power. The size of the country, the tremendous scale of commercial or financial transactions, of industrial operations, of engineering undertakings, and even the fantastic cost of government, have caused the average American to lose his sense of proportion. Unconsciously, size and power have come to outweigh everything else in the public mind.

To the radiologist, apparatus designed to generate roentgen rays is a tool which enables him to produce certain therapeutic effects. To be sure, the quality of that tool is an important factor in the results which he may be able to obtain, but the power of the apparatus in terms of voltage is only one of several qualities which it must possess if the radiologist is to perform high-grade work. A still more important factor in the quality of the radiologist's work has nothing to do with the power of his apparatus, or indeed with the apparatus at all. This factor is the training and skill of the radiologist himself. While high-grade tools are important, the quality of any kind of work depends more on the skill of the worker than on the quality of his tools. If the same tools were given to ten different carpenters, one, who through special aptitude, training and experience has developed exceptional skill, can turn out work far superior to that produced by the other nine. The same is true of radiologists.

The average quality of radiotherapy as it is carried on throughout the country is not as high as it might be, and sometimes it is distinctly low. The quality of the work done by some therapeutic radiologists is mediocre for a number of reasons. Until recent years the emphasis in radiology has been on diagnosis, and many radiologists have given most or all of their time and attention to roentgen diagnosis. The therapeutic aspects of radiology either have been neglected altogether or have received little attention. Owing to the apparently limited field of radiology during the early years of its development, many of the pioneers had no time for treatment; they were too busy making a reputation in the diagnostic field, and their pupils usually followed their example. As a consequence, many roentgenologists in practice to-day

know little about radiotherapy and justify their deficiency by minimizing its importance. When they are called upon to treat a patient, some are not honest enough to admit their deficiency or lack of interest. They proceed to treat the patient, but the treatment often is inferior, and the results are what might be expected under the circumstances.

During the last fifteen or twenty years, however, the rapid increase in our knowledge of the action of roentgen rays and radium on different kinds of living tissue has attracted more and more attention, and it has caused some of the older and many of the younger radiologists to realize that a medical field of considerable scope is in the making. Unfortunately, many have ventured into this field with insufficient technical preparation, or even with an inadequate background of anatomy, physiology, and pathology.

Working as so many do in quarters more or less remote from those devoted to internal medicine or surgery, and sometimes even at a distance, too many radiologists have unconsciously suffered varying degrees of professional isolation and have lost contact with clinical medicine—sometimes to such an extent that they are no longer capable of examining patients. Especially in the field of malignant tumors is this a great misfortune. The radiologist should know at least as much about malignant neoplasms as his medical and surgical confrères, and the more pathology he knows the better. Because he has to deal largely with referred cases, and because many patients come to him with some sort of diagnosis already made, it is all the more important that his knowledge should enable him to confirm the diagnosis, or to modify it more or less by an independent examination. Although this may seem superfluous, it is not rare for clinicians or surgeons to overlook features of a malignant process that may alter the prognosis and treatment considerably.

It has often been my experience to see patients who were suffering from malignant conditions which were eminently amenable to radiotherapy and who, because of improper or inadequate irradiation, had been robbed of the possibility of cure or improvement which might, and in some cases surely would, have followed more thorough treatment. Even when the chance of cure is slight, why throw it away? On the contrary, it is when the chance of cure is smallest that the radiologist should make the greatest effort. But even when the utmost which may be expected is a variable degree of improvement, the radiologist should strive to obtain maximum improvement in the least possible time. It is pitiful to see patients who, because of bungled treatment have been allowed to suffer for months or years from pain or other distressing symptoms which might have been relieved in a short time. Fortunately, the responsibility does not always rest on the radiologist; it frequently rests on the attending physician or surgeon who, not knowing that the symptoms might be relieved by radiotherapy, has not sought the co-operation of the radiologist until the patient's condition has become desperate.

This brings me to the main subject of this paper: When, at professional meetings, or in private conversations among radiologists the discussion turns to the treatment of a given condition, one of the most common questions asked is "what dose do you give?" meaning thereby "what quantity of roentgen rays do you give?" The frequency with which this question is asked shows that, in the mind of the average radiologist, the quantitative dose of rays is the most important factor in the treatment. Moreover, the comparative infrequency with which information on other factors is sought indicates that the quantity of rays is the all-important factor. The quality of the rays as it affects relative absorption at different levels beneath the surface is commonly passed over as of little consequence. Another factor which frequently receives insufficient consideration, and sometimes none at all, is the method or scheme of irradiation. And yet this factor is as important, and sometimes more important, than the quantitative dose of

rays to which the tumor may be exposed.

By method or scheme of irradiation is meant the arrangement of the treatment from the standpoint of the lesion or lesions toward which the treatment is directed—in other words, the number of fields of irradiation or beams of rays, and the direction of the several beams with reference to the anatomic situation and extent of the pathologic process. For example, when the patient has a malignant neoplasm in the mediastinum, a common practice is to arrange the treatment through an anterior and a posterior field, or only through a single anterior field. Even when the malignant process has a considerable degree of radiosensitiveness, the usual result under these circumstances is only slight and transient improvement, or none at all. This method of irradiation is selected because it is thought to represent the method whereby the best possible results can be obtained. And yet this is far from true. Instead of only one anterior field, or instead of an anterior and a corresponding posterior field, more uniform irradiation of an intrathoracic, and especially a mediastinal, tumor can be obtained by arranging the treatment through two anterior and two posterior fields, with the four beams of rays converging as accurately as possible on the mediastinal region in which the growth is situated. When the neoplasm is clearly unilateral, such as is the case with an endothelioma of bone arising from a rib, from three to six beams of rays can be directed on it from the anterior, lateral, and posterior aspects of the corresponding half of the thorax. Of course, the larger the number of fields of irradiation, the more care is necessary to direct the several beams accurately and to arrange the quantitative dose per field and the total dose so as not to cause irreparable injury to adjacent normal structures. The reason for three large instead of six smaller fields in some cases is that, when the tumor is comparatively small, large beams of rays are more certain to include the malignant process in its entirety. With small fields, accurate direction of the beams becomes more difficult. The larger the neoplasms, the greater the number of fields through which the treatment can be given with greatest effectiveness.

It matters not whether the treatment is given within a few days (from three to twelve) or whether a smaller fraction of dosage is given daily or twice a day for a long time (from 15 to 60 days); the importance of the method of irradiation (anatomic arrangement) is just as great in the one case as in the other.

Another patient may be referred with a clear diagnosis of actinomycosis of the abdominal structures, of tuberculous peritonitis, or of lymphoblastoma affecting the retroperitoneal nodes. In such cases the secret of therapeutic success does not lie in the largest possible total dose of rays. On the contrary, too large a total dose would tend to defeat the purpose of the treatment. The main requirement is uniform exposure of the abdominal structures or of the abdominal nodes to a moderate quantity of rays or at least to a sub-erythema dose. In the first two of the three conditions mentioned the quantitative surface dose per field should not exceed 75 per cent of the tolerance dose. Doses larger than this may cause enough reactive inflammation to increase the activity of the disease. In treating lymphoblastoma, also, the quantitative dose should not be sufficient to induce erythema of the overlying skin but should be higher than in the case of the two other diseases (85–90 per cent). To employ too large a dose is to risk producing, in the connective tissue of the hyperplastic lymph nodes, an inflammatory reaction which would cause the nodes to become less sensitive to irradiation in the future. The increased resistance to irradiation observed by some radiologists is largely due to excessive dosage.

In order to irradiate the abdominal structures as uniformly as possible, the best method is to divide the anterior half of this part of the trunk, from the level of the xiphoid cartilage to the pubic region and from one mid-axillary line to the other, into four fields of equal size, with the navel as the

common center. The beam of rays should be directed so that the central axis of the beam will be perpendicular to the center of each of the four fields. The posterior aspect of the abdomen should be divided into four corresponding fields. When, as in lymphoblastoma, the aim should be to concentrate the rays on the nodes on each side of the aorta and vena cava and along the spine, the several beams should be directed more sharply inward, so that the beams from the two sides converge from front and back on the structures along the spine and immediately in front of it.

When the patient is suffering from metastasis to the para-aortic nodes, secondary to carcinoma of the testis, bladder, prostate gland, uterus, ovary, or rectum, the same arrangement should be employed, but the dose per field, and hence the total dose, should be increased as much as possible. This can be done to best advantage by fractional irradiation, with small daily doses continued for from 30 to 50 days.

When the therapeutic problem consists in delivering to a malignant tumor involving the upper end of the humerus a large total dose of rays, and at the same time to provide for uniform irradiation, the region of the shoulder can be divided into four or six fields, the dividing line between the upper and lower fields passing transversely or obliquely through the center of the growth as determined from roentgenograms. In this way the dose per field need not be extreme; and yet, if the several beams of rays are made to converge accurately from above and below and from the anterior, posterior, and superior aspects of the shoulder, the total dose delivered to the neoplasm will be greater and the resulting regression will be more rapid than if a much larger surface dose of rays is given through only two fields.

The same principle applies to tumors in the shaft of the humerus and in the bones of the lower extremity, pelvis and spine. On the whole, the method of irradiation or anatomic arrangement of the treatment is more important than the quantity of rays given to any one field. In fact, it is to ignorance or neglect of this principle, or to carelessness in applying it, that the mediocrity of much present-day radiotherapy is due. Not infrequently, when the anatomic arrangement or method of irradiation is well planned, treatment of relatively superficial lesions with rays generated at 200 kilovolts proves less effective than treatment with rays of longer wave length.

There is no doubt that the more attention is given to the anatomic plan of treatment with relation to the lesions present, the better the results which may be expected. I am thoroughly convinced that this factor in radiotherapy is as important as the quantitative dose; this, however, may be arranged with reference to the time factor.

STUDIES ON THE PROBLEM OF MITOGENETIC RADIATION[1]

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PART I.—(OTTO GLASSER)

EXPERIMENTS on mitogenetic or Gurwitsch radiation have been conducted in the Department of Biophysics of the Cleveland Clinic Foundation for the past seven years. A study of the whole problem of this type of radiation and a discussion of some of our results were published recently (1,2). Our observations did not confirm those reported by Gurwitsch and his co-workers. Fortunately, Hans Barth, who has obtained positive results in direct collaboration with Gurwitsch, is now continuing his studies on the mitogenetic radiation in our laboratory and will present his observations in the second part of this paper.

The chief problem concerning mitogenetic radiation primarily consists in discovering or devising reliable methods for detecting its presence. We have worked with both physical and biological detectors. Naturally, it is desirable to utilize physical methods and we, therefore, first employed a photographic method, then the photoelectric Geiger-Müller counter tube. We soon abandoned the photographic method as being unreliable. Our Geiger counter tube method has been described in a previous communication (1). In brief, it consists of a cylindrical tube connected through a multi-stage vacuum tube amplifier to a magnetic counter, a loud speaker, and a ticker tape recorder. The plate materials were selected for sensitivity to short ultra-violet radiation and have included Cd, Zn, Sn, Au, Ni, and Pt. The "senders," which are supposed to emit mitogenetic radiation, were placed over the quartz window of the counter tube in quartz vessels. Control counts were made by interposing a glass window during alternate periods, all other conditions remaining the same.

Since biological detectors have been employed by many investigators of mitogenetic radiation, we also conducted experiments with yeast as a biologic detector at the same time that we were employing the photo-electric counter tube. At first we used cultures of *Saccharomyces cerevisiæ* and *S. ellipsoideus* in Sabouraud, Williams', and beer-wort media. Day-old cultures of yeast in quartz and glass test tubes were exposed to various "senders." After incubation overnight at 28° C., the volume of yeast was determined by centrifugation in mycetocrit tubes. Counts made with a hemacytometer supplemented the volume determination. Various cell concentrations were employed for exposure in an effort to determine the optimum stage of culture development.

About two years ago, we revised our yeast method following the receipt of two strains of yeast from the laboratories of Gurwitsch, in Leningrad. Cultures of the yeast were prepared on beer-wort-agar or in liquid beer-wort in strict conformity with the procedures Gurwitsch outlined. Determinations on liquid cultures were made by centrifugation five or six hours after exposure. The agar beer-wort cultures were homogeneous at the time of exposure and could be detected only microscopically. After a period of incubation not exceeding two hours, the yeast was gently removed with a loop, fixed on a glass slide, and stained with methylene blue. The percentage of small buds was then counted in groups of one thousand unselected cells.

In the experiments with yeast, we found the mycetocrit centrifugation method less subject to personal error than the bud-counting method. However, the Russian workers emphasize that an increase in

[1] Read at the Fifth International Congress of Radiology, Chicago, Sept. 13–17, 1937.

buds is more directly related to the mitogenetic effect than an increase in volume. The sources of radiation or the "senders" which we investigated may be divided into three categories: biological, chemical, and physical. The biological materials included active-growing suspensions of yeast or bacteria, onion roots and pulp, blood, freshly incised rat carcinomas without necrosis, and tumors removed at operation and suspected of being malignant. Three chemical sources were used: the peptic digestion of fibrin, the reaction between potassium permanganate and hydrogen peroxide, and the oxidation of tissue extracts or of yeast suspensions. These two classes of "senders" were tested with both the yeast detector and the photo-electric counter tube.

In order to determine the effect on yeast cultures of artificial ultra-violet light from controllable sources, we used a water-cooled Kromayer quartz lamp and also a Westinghouse ultra-violet lamp with Slack window. Studies were made with the total radiation, with monochromatic radiation, and with radiation interrupted by a revolving disk. In addition, we employed crystalline sodium chloride which had previously been exposed to roentgen rays (3). This salt, when irradiated, will subsequently give off weak ultra-violet radiation with an emission maximum at 2,450 Å., in the presence of visible light. The intensity of this radiation, which can easily be detected with the photo-electric Geiger-Müller counter, can be made to approach the low intensities claimed for the mitogenetic radiation. Cultures of yeast were exposed to the ultra-violet emission from irradiated salt crystals.

The results of our investigations with both physical and biological detector methods may be stated briefly. The counts obtained with the photo-electric counter exposed to biological or chemical materials as previously described did not fall outside the limits of fluctuation in the control of background counts. In the experiments with yeast, an apparent increase in growth rate was noted occasionally but, for large series of observations, fell within the range of variation in the control cultures. All in all, our experiments thus far failed to confirm the observations concerning the existence of mitogenetic radiation as reported by Gurwitsch and his co-workers.

PART II.—(HANS BARTH)

After publication of the investigations of Rajewsky (4) and Frank and Rodionow (5) on the detection of mitogenetic radiation with physical light counters, I repeated their experiments at the Physical Institute of the University of Munich, using an apparatus which was essentially the same as that employed by Frank and Rodionow. At first I used as "senders" the chemical reaction between ferrosulphate and potassium bichromate and also several albumin reactions such as Gurwitsch had suggested. After a few preliminary experiments on the construction of sufficiently sensitive counter tubes, I was able to report (6, 7) definite and reproducible effects of various "senders" upon the counters. Control experiments showed that the effects were produced by ultra-violet light and not by any other influence upon the measuring apparatus.

It was of interest at that stage to continue these experiments in closer co-operation with a biologist. This was made possible by the kind invitation of A. Gurwitsch to work in his laboratory in Leningrad. Then the experiments were extended to include three other possible sources of radiation, namely, carcinoma in Ringer glucose, aluminum dissolved in hydrochloric acid, and glucose as a secondary radiator.

The detailed results of these experiments have been reported (8), therefore, only a short résumé will be given now. All of the "senders" were tested in a large series of experiments and were found to produce definite and positive effects which lay outside the statistical error. The cathodes used in the counters were made of aluminum, copper, or iodine compounds of copper and silver.

Similarly, large series of control experiments were carried out, such as interposing quartz and glass between the radiator and the counter, testing with one or the other component of the chemical reaction the decrease of the light sensitivity of the counter, there was also a decrease in its indication of the mitogenetic effect. Clean aluminum or copper cathodes oxidize in air; therefore, they could be used for only

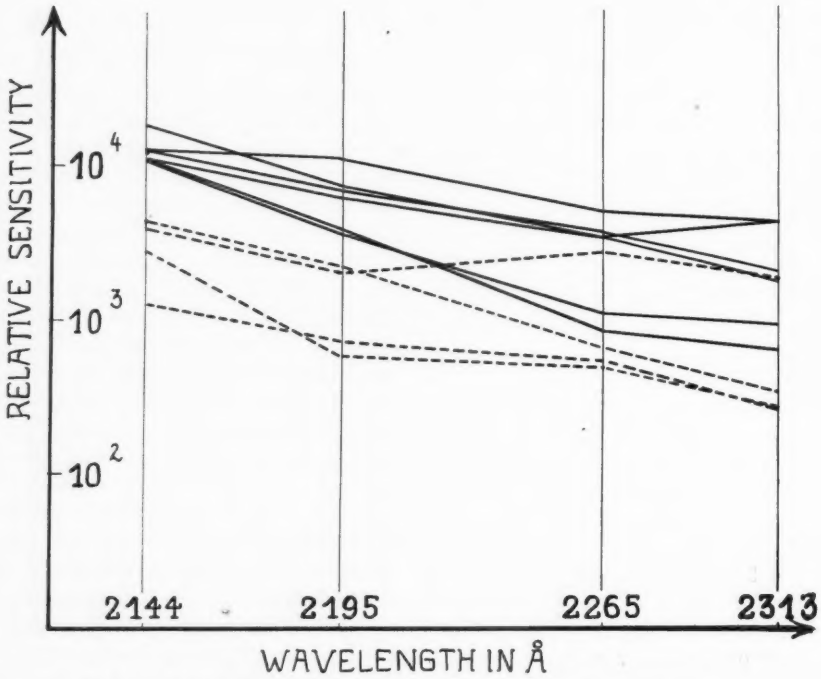

Fig. 1. Relative sensitivities of ten counter tubes for various wave lengths.

only, or by replacing the chemical solutions by water. Exceptionally large variations were made in the experiments with glucose, and here the effects of the primary radiation sources could be shown even at large distances. The results of these control experiments also showed that the observed effects must have been due only to ultra-violet light and not to any other effects upon the measuring apparatus such as static electrical charges or vapors from the preparations used.

In addition to these experiments an attempt was made to obtain further information concerning the photo-electric properties of our counters. The results have not been published and will be discussed in brief at this time. In our first experiments we had observed that, in accordance with a few hours when the counters contained air but, when the counters were filled with hydrogen or argon, they could be used for as long as two weeks.

In order to make satisfactory comparisons of the sensitivity of our counters toward mitogenetic as well as artificial sources of radiation, we constructed a special apparatus consisting of a quartz double monochrometer and a small but extremely constant cadmium spark. A large series of comparative experiments was carried out last year by Philippow (9). Figure 1 shows a series of his measurements on ten counters of identical construction with copper or aluminum cathodes. The ordinates represent relative sensitivities for the wave lengths 2,144, 2,195, 2,265, 2,313 Å. In addition, an experiment was

made with each counter, using the reaction between ferrosulphate and potassium bichromate, according to Braunstein and Pototzky. The sensitivities of those counters which showed definite effects with the chemical reaction (as shown in the unbroken lines in the figure) lie considerably above the counters (indicated by broken lines), showing none or only doubtful effects with the chemical reactions.

Furthermore, it can be seen that, at about 2,100 Å., the sensitivities of our good counters are almost identical. For longer wave lengths, however, the differences vary to such an extent that they also would have appeared clearly in the experiments with the chemical reactions had such longer wave lengths been present. Since all effects we obtained with the chemical reaction are between 20 and 30 per cent, we must conclude that, above 2,200 Å., our counters are not sensitive enough to detect those radiations of wave lengths up to 2,450 Å., which have been observed by various biologists. This probably explains many difficulties which have been encountered in previous intensity measurements which were made on the supposition that the counters were sensitive up to 2,500 Å.

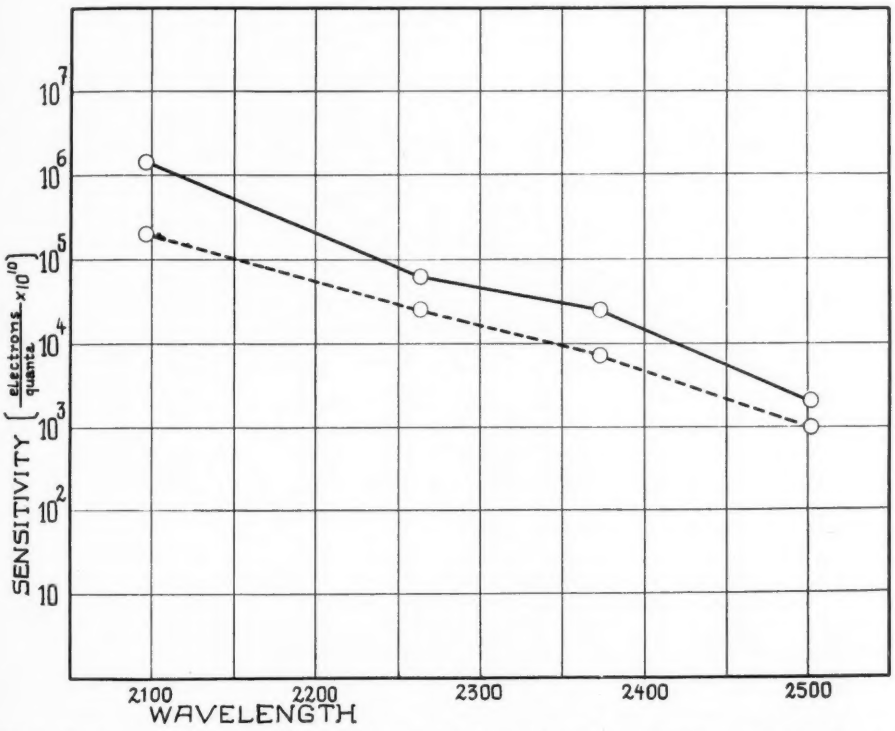

Fig. 2. Sensitivity of a "mitogenetic sensitive" and an insensitive counter tube for various wave lengths.

I also made preliminary attempts to measure these intensities in absolute units. Without discussing the details of the technic used, I should like to present the results (Fig. 2). We measured again a "mitogenetically sensitive" and an insensitive counter and the same variation in sensitivity appeared again in measurements with an artificial source of radiation. It is about tenfold.

The results of the experiments with the chemical reaction together with the sensitivities for 2,100 Å. are shown in Table I. The sensitive counter registered 0.5 count per minute with the reaction, and the dif-

ference compared to the zero reading of the second counter lies outside the error. A threefold variation of the control experiments always led to exactly the same results.

The problem of intensity still seems to present certain difficulties in regard to the explanation of our experiments. For instance, the intensity measured for the mitogenetic radiators was found to be at

TABLE I

Sensitivity to the chemical reaction $K_2Cr_2O_7 + FeSO_4$ and to ultraviolet light.

Nr.	Total Number of Counts	Minutes	Counts in 1 Minute with Effect	without Eff.	Difference	Sensitivity for light (2100 Å)
I a	620	220	3.1	2.6		
I b	600	220	3.1	2.5		
I c	800	269	3.3	2.7		
Total:	**1620**	**584**	**3.12**	**2.63**	**0.49 ± 0.13**	**$1.4 \cdot 10^{-4}$**
II a	800	169	4.8	4.7		
II b	600	140	4.3	4.3		
II c	600	138	4.4	4.3		
Total:	**2000**	**447**	**4.49**	**4.43**	**0.06 ± 0.18**	**$2.1 \cdot 10^{-5}$**

The sensitivity of the good counter amounts to about 10^4 quanta per electron at 2,100 Å. This corresponds to a radiation energy for the reaction of about 10^3 quanta per square centimeter and second, if we assume that only light near this wave length has acted upon the counter.

It was thus shown that the mitogenetic radiators affect only those counters which have the highest ultra-violet sensitivity obtainable. Our experiments with mitogenetic radiation sources gave a complete confirmation of the results which Gurwitsch and his collaborators obtained in similar experments with biologic detectors. In our experiments, the influence of glass and quartz was identical with that obtained with ultra-violet light.

the lower limit of the intensity needed to explain many biological results. On the other hand, the physical experiments which produced negative results show that the intensity of the radiation probably cannot be very much greater, otherwise the proof of its existence would not be particularly difficult. Yet, according to the results obtained so far with such radiators, one must expect that intensities of different radiation sources vary widely among themselves.

One can easily assume that this discrepancy is only an apparent one and that its causes can be explained by the almost complete lack of quantitative measurements and of sufficiently accurate calibrations of counters. Further experiments

must show whether this is correct or whether other unknown factors play an important rôle.

CONCLUSIONS

Since numerous investigators have arrived at contradictory results concerning the existence of the mitogenetic radiation, we suggest that a thorough study of both the measuring methods and the character of the radiation sources be carried out by direct collaboration of various laboratories. We are at present attempting to make a direct comparison of measuring methods based on the work presented above and we hope to arrive in this manner at some definite conclusion in regard to the problem of mitogenetic radiation.

The authors wish to express their appreciaton to Professor A. Gurwitsch, of Leningrad, for his continued interest in these investigations, and to Miss Margaret Schott, and Mr. I. E. Beasley, who have carried out a great many of the experiments.

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X-RAY STUDY IN RELATION TO THE MANDIBULAR JOINT SYNDROME[1]

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THE object of this presentation is to correlate the roentgenological findings of temporo-mandibular joint pathology other than acute infections, fractures, dislocations, specific diseases, malignant lesions, or acute trauma changes.

Fig. 1.

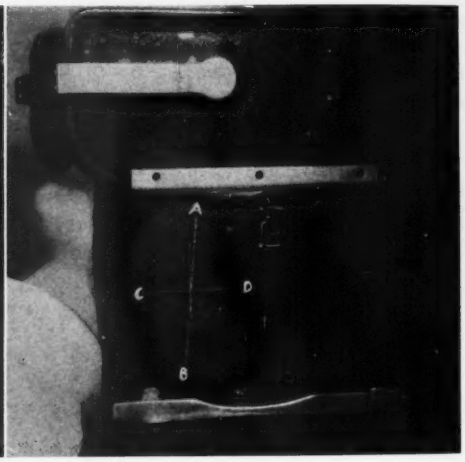

Fig. 2.

Fig. 1. The apparatus employed for the fixation of the head in the reclining position on a horizontal table (Bullitt), the beam angles having been modified to meet the needs for the examination of both temporo-mandibular joints at known fixed and reproducible angles in relation to the auditory canal landmarks and the base line of the skull. Throughout the examination the head remains fixed, but the tube may be shifted to the right and left sides of the skull, either for the single bilateral or stereoscopic exposures.

Fig. 2. Close-up view of the cross-marks on the transparent window in relation to the auditory canal and the base line of the skull. *A-B*, Base-line position inclined 5° as shown above. *C-D*, Horizontal cross-line through external auditory meatus.

The disposition of structures which make up the temporo-mandibular joint, the condyle, the meniscus, the glenoid fossa, the forward limiting articular tubercle, accounts for the regular spacing of bone outlines which is purely relative. The exact distance between the surface of the condyle and any sector of the curve of the glenoid fossa varies widely with the individual. However, in the normal joint, with the condyle at rest in the closed position of the jaw, the space between its surface and the tympanic plate, or the glenoid fossa, is uniform, slightly narrower next to the tubercle. Even in the open position the same space appears between the condyle and tubercle, to account for the intervening meniscus (1).

The ultimate position of the condyles being determined by occlusion during physiologic rest of the jaw, malocclusion of the teeth, or loss of the teeth initiate the first changes toward pathologic reaction within the joint. With the first irregular movement of the condyles, long before pain

[1] Presented before the Fifth International Congress of Radiology in Chicago, Sept. 13–17, 1937.

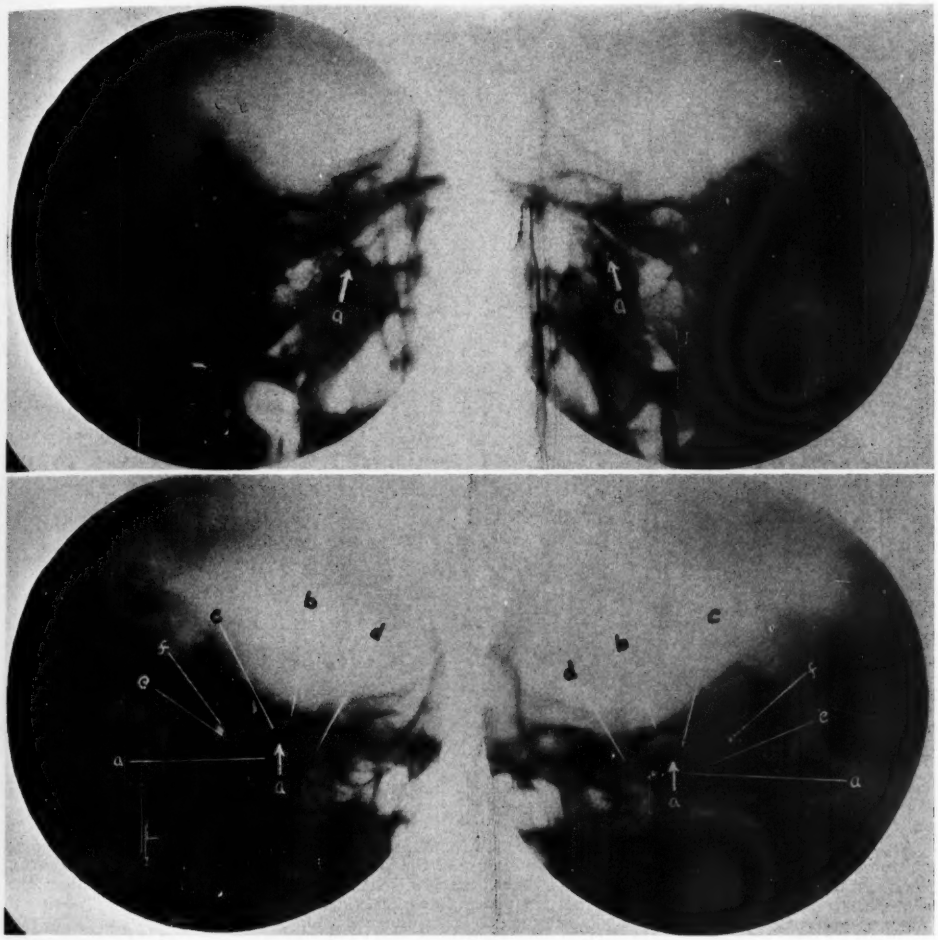

Fig. 3 (*above*). Normal mandibular joint. *A*, Condyle during the open position of the jaw.
Fig. 4 (*below*). Normal mandibular joint. *A*, Condyle at rest in the closed position of the jaw; *B*, The glenoid fossa; *C*, Meniscus; *D*, Articular tubercle; *E*, Tympanic plate; *F*, External auditory meatus.

effects are noted, irritation of sensory nerves within the capsule produces trismus of the jaw muscles, and uneven pressure is exerted upon the meniscus and other jaw structures.

The auriculo-temporal nerve passing intimate to the joint is subjected to pressure; reflex neuralgias appear in other branches of the fifth nerve, and burning pain is referred deeply about the ear, to the vertex, about the eye, and along the border of the tongue throughout the area supplied by the lingual nerve (2). These symptoms do not long remain mild. The patient seeks relief for supposed disease of the eyes and sinuses, and when burning of the tongue is established, lives in constant dread of cancer of the tongue (3). In a large percentage of burning tongue cases, inhibition of saliva occurs as a result of some complex effect of the combined irritation of the chorda tympani and auriculo-temporal nerves, both being within range of the aberrant condyle. Symptoms of catarrhal deafness are found in widely overclosed, edentulous cases, the effect of wrinkling and

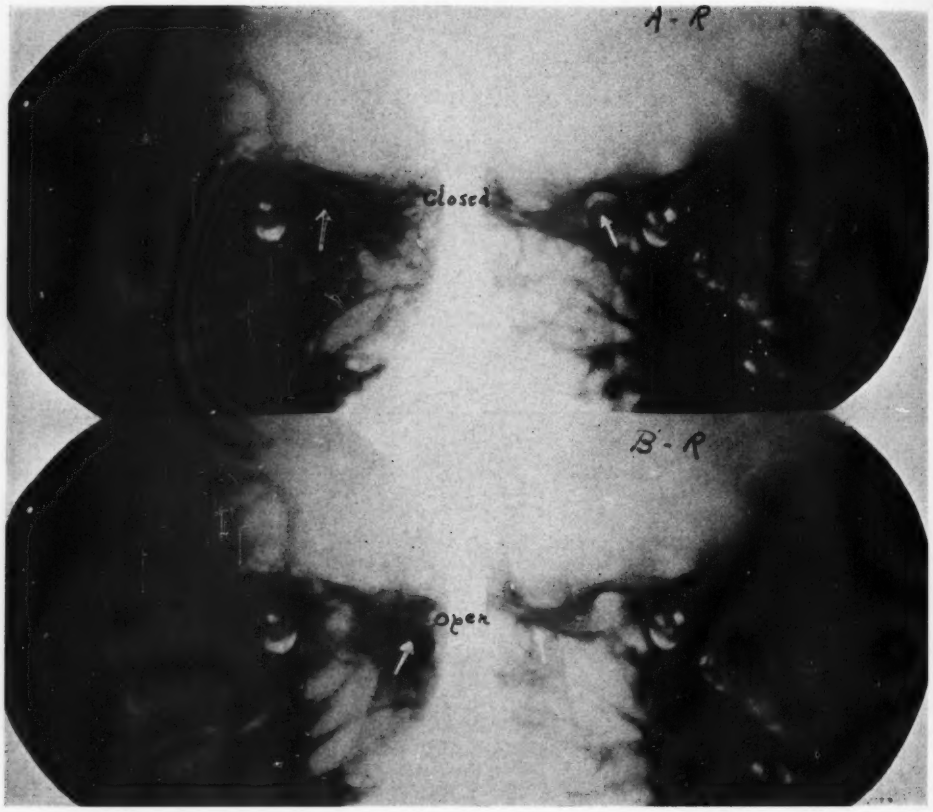

Fig. 5. Lax temporo-mandibular joint. Case 1, Mrs. B., aged 54. *Clinical Symptomatology.*—Grinding noises in ears and slipping of jaw backward on closure of the jaw for past three years. Taste disturbance, "copper" taste, and dryness of mouth at all times. Intermittent impairment of hearing, but hearing tests showed only very mild degree of catarrhal deafness. Edentulous mouth for ten years. *Roentgenological Findings.*—Extreme anterior excursion of the condyle to the tubercle; normal position and absence of erosion of the condyles within the glenoid fossa. *Treatment.*—Dental plates replaced, opening the bite. *A-L,* Closed position, left mandibular joint; *A-R,* Closed right mandibular joint; *B-L,* Open left mandibular joint; *B-R,* Open right mandibular joint.

compression of soft tissue structures bordering the Eustachian tubes. Tinnitus, such as low buzzing common to catarrhal deafness, or snapping and grating from uneven destruction of the meniscus, is commonly present (2). The series of changes, encouraged by gradual loosening of the capsule, is complicated by voluntary efforts to adapt the jaw comfortably to chewing movement. The meniscus becomes thinner at its thinnest spot where the face of the condyle impinges upon the tubercle—Axhausen (4), Steinhardt (5)—and the peak of the trismus occurring here, perforation ensues. The anterior aspect of the condyle and the posterior surface of the tubercle undergo erosion. Inflammatory reaction is constantly present, exaggerates the trismus, accounts for the tenderness to palpation of the joints, and roentgenologically increased density of the capsule is the usual finding. The condyle finally assumes abnormal rest positions within the glenoid fossa, commonest of which is forward against the tubercle.

In view of the foregoing, it is self-evident that accurate and standardized roentgenologic methods for examining the tem-

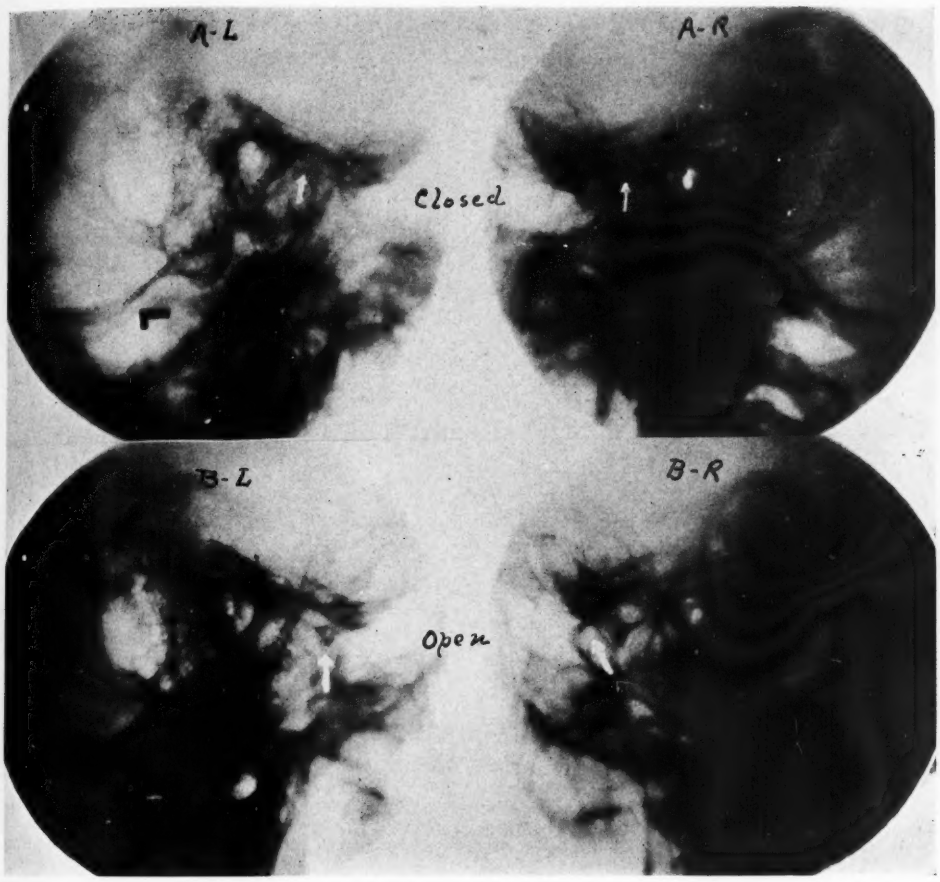

Fig. 6. The mandibular joint with arthritic changes to the extent of partial or complete ankylosis. Case 2, Mr. K., aged 35. *Clinical Symptomatology.*—Crackling noise and sharp boring pain within the left ear for past two years, and stiffness of jaw movements since forceful reduction procedure for malocclusion at the age of 12. Pain radiates to zone about the left eye. *Roentgenological Findings.*—Hazy joint outlines, increased on the left; face of condyle flattened; glenoid fossa angulated by erosion; joint space extremely narrow. *Treatment.*—Full mouth reconstruction by thin overlays on natural teeth, extend vertical molar dimension on left. *A-L,* Closed position, left mandibular joint; *A-R,* Closed right mandibular joint; *B-L,* Open left mandibular joint; *B-R,* Open right mandibular joint.

poro-mandibular joint are indispensable toward an early and correct diagnosis and of equal value to the subsequent and proper treatment thereof. The roentgenologic difficulties of satisfactorily outlining the joint relationships and movements are many but nevertheless remain largely anatomical problems. The many superimposed bone structures further handicap the proper projection of the mandibular joint upon the x-ray film. Valuable contributions have been presented in this direction by National and Continental observers, including Sproull (6), Higley (7), Bishop (8), Lindblom (9), Altschul (10), Riesner (11), and many others.

The various technical x-ray approaches relative to the mandibular joint studies include a variety of anteroposterior, oblique, and lateral examinations. A true exposition of the relationships of the articulating surface of the temporo-mandibular joint is not obtainable in the usual routine inferior lateral view of the ramus of the lower jaw. In addition to other disadvantages, the extreme oblique methods of ex-

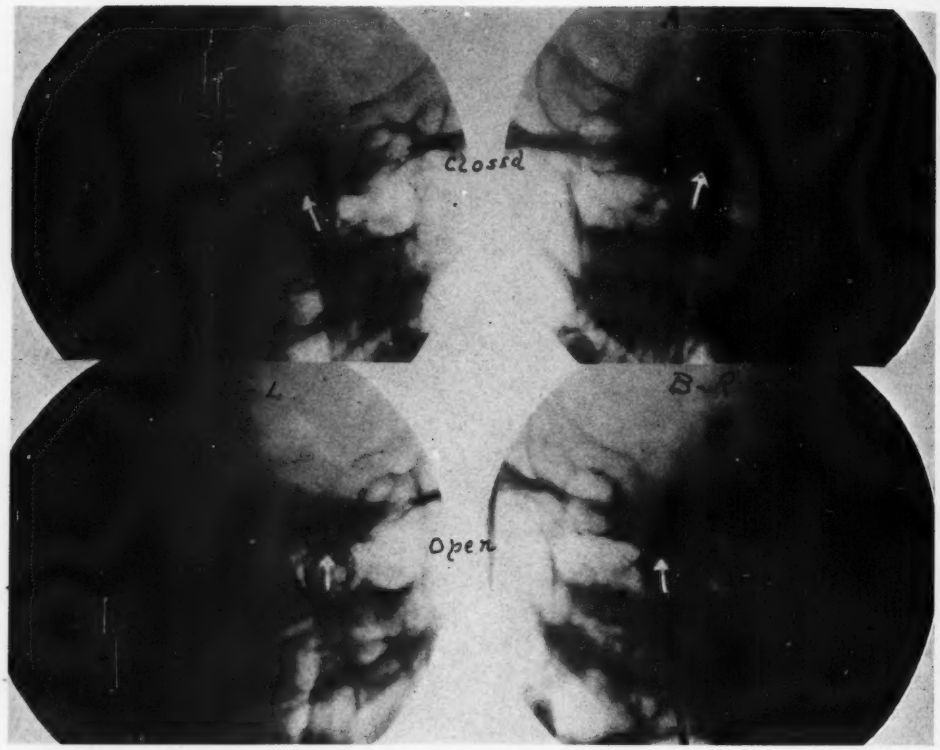

Fig. 7. Erosion of the meniscus with marked joint or condylar changes. Case 3, Mr. O., aged 63. *Clinical Symptomatology* (with pain symptoms).—Tinnitus and impaired hearing, involving right, then left, side, for ten years—exaggerated when new dental plates were acquired one year ago. Burning along right side of tongue during above period, with marked dryness of mouth. *Roentgenological Findings.*—In the closed position, the condyles rest flush against the tubercle, showing evidence of perforation of the meniscus; erosion and flattening of the anterior surface of the condyles—more marked on the left; open position shows slight restriction of movement of condyles. *Treatment.*—Dental plates replaced, increasing vertical molar dimension slightly, and closing incisors, thus moving condyles straight backward in their closed position. *A-L,* Closed position, left mandibular joint; *A-R,* Closed right mandibular joint; *B-L,* Open left mandibular joint; *B-R,* Open right mandibular joint.

amination unfortunately increase the problem of distortion of the joint structures. The various modified lateral views, especially those made stereoscopically, have been most helpful when the involvement is moderately well advanced. In our experience, "the method of angulating or rotating the head" to the required angle in combination with a fixed or stationary x-ray beam may frequently influence the accurate projection of the condyle and fossa and thus alter their respective relationships (7). Therefore, bilateral exposures should preferably be made with the patient's head at absolute rest and fixed in a known position during the open and closed studies of the right and left mandibular joints.

The intersection of the base and horizontal lines on the celluloid windows (Fig. 2) will serve as the centering points for localizing the respective right and left auditory canals. The head is then firmly clamped face upward. The base line of the patient's head, namely, a line through the auditory canal and external canthus, should be angulated 5° in the direction of the vertex of the skull. This latter procedure is essential for obtaining the necessary clear outlines of the fossa and articular

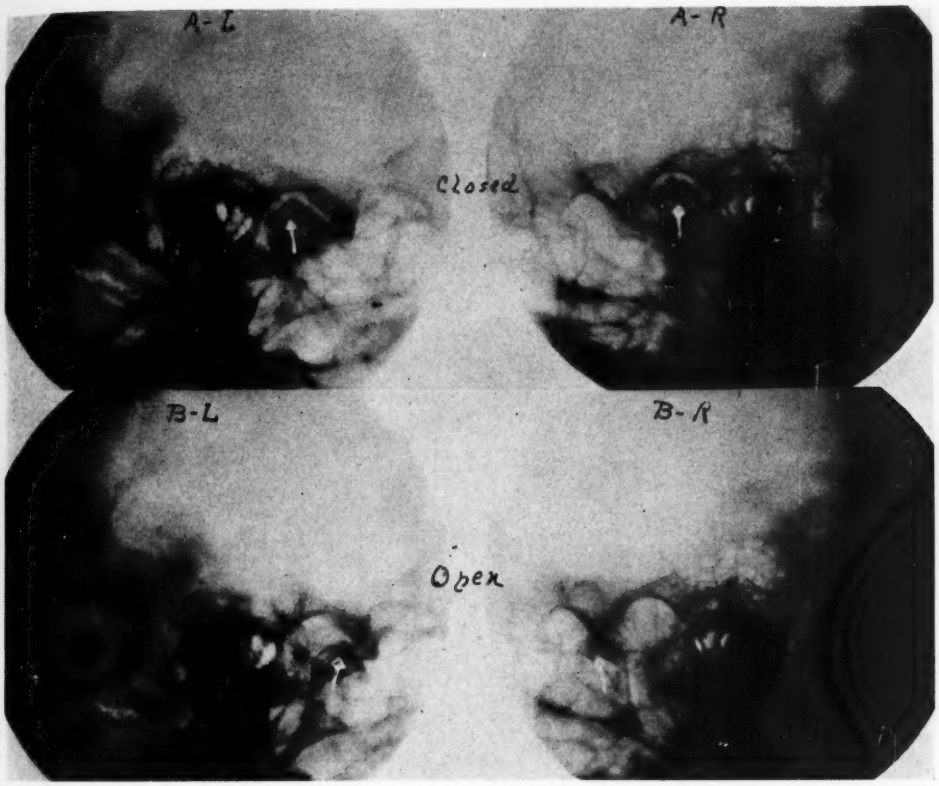

Fig. 8. Erosion and flattening of the face of the condyle and the posterior aspect of the tubercle. Case 4, Mrs. S. N., aged 55. *Clinical Symptomatology.*—Pain deep within and about the ears for from 15 to 20 years, appeared on left side, then shifted to right, two years ago it extended to a peri-oral burning or dryness. Extensive studies ruled out any blood dyscrasia or neurological lesion. *Roentgenological Finding.*—Erosion and flattening of the face of the condyles, with co-ordinate angulation of the glenoid fossa, more marked on the left; limitation of excursion of condyles in open position. *Treatment.*—Treatment dentures to replace absent molar teeth, extending vertical dimension slightly more on the left than the right side. *A-L,* Closed position, left mandibular joint; *A-R,* Closed right mandibular joint; *B-L,* Open left mandibular joint; *B-R,* Open right mandibular joint.

tubercle. The x-ray beam on this apparatus should be checked so that the projection is centered upon the opposite meatus at the cross-lines on the celluloid window, the x-ray tube being angulated 20° superior to the meatus and toward the feet through the posterior area of the temporal bone. The apparatus (Fig. 1), described by Bullitt (12), for stereoscopic mastoid examinations may be modified for this purpose as described above, and thus serve a dual purpose. The upper bracket of the tube position is the preferred procedure in order to obtain the desired diagnostic projection upon the radiogram. The head or auditory meatus landmark should be half an inch lower than the usual mastoid position along the base line or below the cross-marks as observed at the celluloid window (Fig. 2) when the mandibular joint is examined. All of these angles pertain to the patient in a recumbent position.

The head is easily raised or lowered by means of an elevating table so as to facilitate the localization of the respective auditory canals to the cross-marks on the vertical windows. This assures the accurate reduplication of subsequent exposures

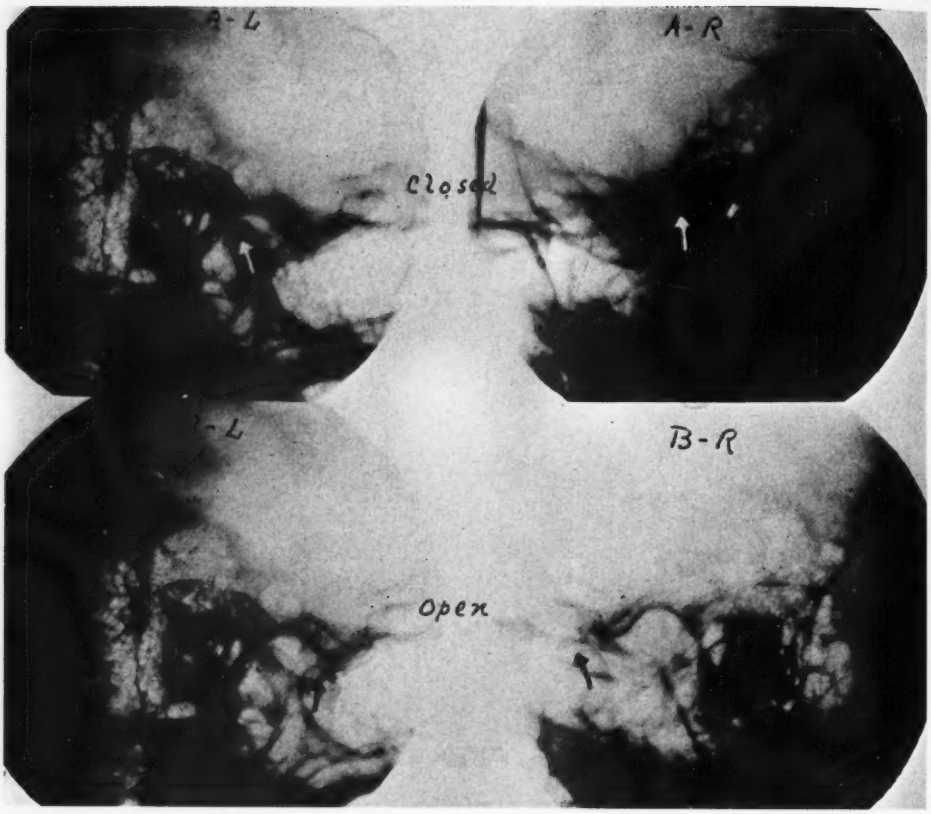

Fig. 9. Destruction of the condyle and part of the meniscus (with "snapping only," otherwise no early symptoms or pain). Case 5, Miss K., aged 18. *Clinical Symptomatology.*—Stiffness in jaw muscles for past year, relieved by massage, but persistent, and since onset the patient has had grinding noise within the left ear. *Roentgenological Findings.*—Some erosion of the face of left condyle, which rests backward against the tympanic plate, and shows limitation of motion in the open position; the right condyle shows abnormally free excursion. Complete horizontal impaction of both lower third molars, more marked on the left side. *Treatment.*—Extraction of impacted unerupted third molars. To await a time for relief of trismus from this source, before any treatment for position of the jaw. *A-L,* Closed position, left mandibular joint; *A-R,* Closed right mandibular joint; *B-L,* Open left mandibular joint; *B-R,* Open right mandibular joint.

of the temporo-mandibular joint structures for the necessary comparative studies of possible articulation surface and condylar marginal changes. Another distinct advantage of this method is the incorporated swivel arrangement for the bilateral shifting of the tube from one side to the other at known fixed positions or projection angles which cannot be changed without taking the entire apparatus apart. All of these tube angulations or shifting of the beam of x-ray in relation to the right and left mandibular joints can be accomplished without changing the position of the patient's head during the entire examination. This degree of standardization of the roentgenologic technical procedures in the examination of the temporo-mandibular joint has been most helpful, both from the diagnostic and treatment standpoint and invaluable for subsequent roentgen follow-ups.

SUMMARY

1. Realizing the indispensable aid offered by x-ray studies in questionable temporo-mandibular joint involvements, this correlation of our present roentgenologic and clinical observations and findings

is presented for consideration and discussion.

2. All stages of pathologic change within the temporo-mandibular joint, relaxation or ankylosis, impaction of the condyle, erosion of structures, and bone destruction, may be defined by roentgen study, except mesial displacement.

3. Varieties of change of the joint structures may be classified into groups, whose clinical observations, neuralgias, and ear symptoms are typical and correspond with changes seen in actual sections of the joint.

4. The x-ray method described for the examination and guide to treatment of temporo-mandibular joint pathology has fulfilled in almost every respect the essential technical and practical requirements of accuracy, flexibility, and reduplication of serial exposures.

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THE PATHOLOGIC REACTIONS WITHIN THE ANATOMIC UNIT OF THE LUNG

THEIR ROENTGEN PORTRAYAL, CLASSIFICATION, AND DIAGNOSIS[1]

By W. WALTER WASSON, M.D., *Denver, Colorado*

I. The roentgen portrayal of the pathologic reactions within the anatomic units of the lung is dependent upon certain factors:

(*a*) Without air there is no differentiation of tissue. This is especially exemplified in the newborn infant's chest where no air has entered the lungs. The lungs cast the same shadow upon the film as any other unaerated tissue of the body. In such tissue only very dense structures such as calcified nodes or osseous structures will cast a shadow which can be differentiated from the surrounding tissue.

(*b*) Any increase or decrease of the air content of the anatomic units, if of sufficient amount, can be portrayed upon the film. It must be remembered that the anatomic units are not only the aerating structures of the lung but contain the largest volume of air. The air within these units surrounds the larger and denser structures of the lungs and brings them into relief. The increased air content, such as either general or localized emphysema, is readily detected on the roentgen film, while, on the other hand, the decreased air content of the lungs is one of the early signs of silicosis or any interstitial fibrosis.

(*c*) Any structural change which increases or decreases the air content of the air sacs and bronchioles, will be portrayed on the film, either by its decreased density or its increased density, providing it is surrounded by other air sacs which are well aerated. Most of the structural changes show an increased density, as bronchopneumonia, but there are a few structural changes which show a decreased density, as bronchiectasis or localized emphysema.

(*d*) In the healthy lung only the larger structures, such as the arteries and bronchi, are seen upon the film. In other words, the anatomic units consisting of the air sacs, terminal bronchioles, the smaller arteries and their capillaries, and the veins are not portrayed. Their structures are too delicate to cast any shadows, and furthermore the air content of these units tends to blot out some of the larger bronchi, arteries, and lymphatic structures, as they approach the anatomic units.

II. The pathologic reactions within the anatomic units:

(*a*) Pathologic reactions within the anatomic units can take place in either the bronchioles and their air sacs, the arteries, veins and their capillaries, the lymphatic system, or the supporting connective tissue framework for these structures. In a lesion of sufficient size to be seen on the roentgen film, all of these anatomic structures are most certainly involved. In the usual clinical case with inflammatory reactions an involvement of one or more secondary lobules is necessary for roentgen portrayal or to produce clinical symptoms. William Snow Miller estimates that there are from 50 to 250 anatomic units in a secondary lobule and that a secondary lobule will measure from 1.5 to 2.5 centimeters in diameter.

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[1] Presented before the Radiological Society of North America, at the Twenty-second Annual Meeting, at Cincinnati, Nov. 30–Dec. 4, 1936.

(*b*) The pathologic reactions within the respiratory bronchioles and their air sacs.

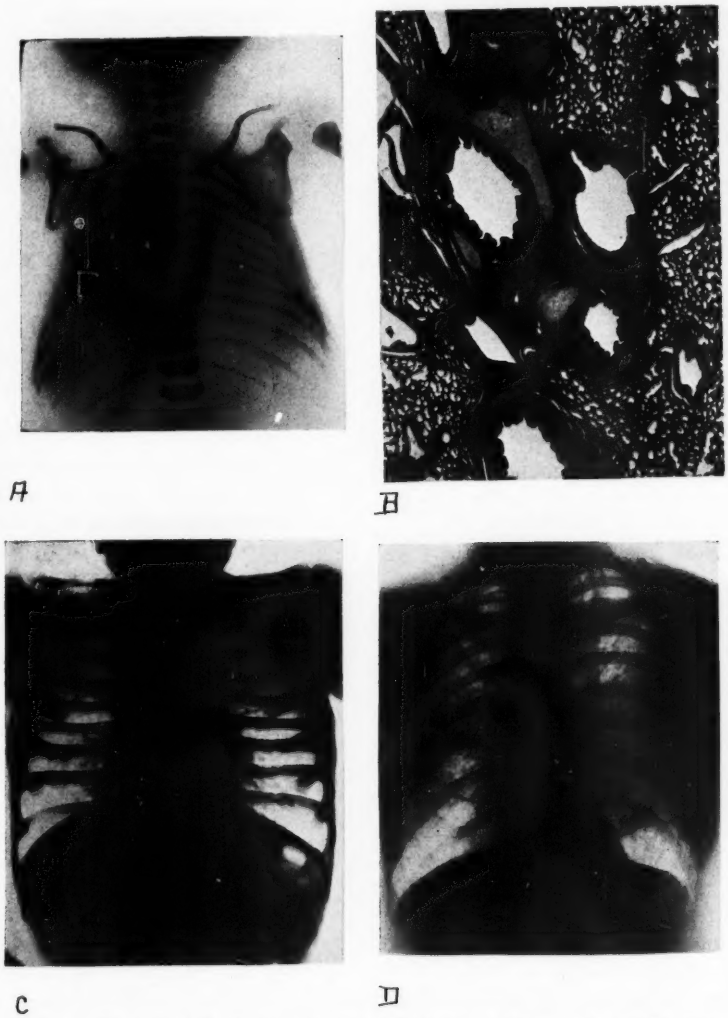


Fig. 1. These reproductions are shown to illustrate the influence of aeration upon roentgen portrayal of pulmonary anatomy, and that a decrease or increase of air content may be demonstrated.

1-*A*. Stillborn infant with no pulmonary aeration and no pulmonary differentiation of tissues.

1-*B*. Microscopic section of bronchi and arteries bound together by connective tissue and surrounded by air within the pulmonary air sacs.

1-*C*. Acute emphysema in a child with a relative increase of the air content in the bases.

1-*D*. Early silicosis in an adult with a decrease in the relative air content.

The pathologist describes such reactions as bronchiectasis, or emphysema, both producing dilation of the air sacs and of the bronchial lumen but entirely different in their pathologic appearance and in their pathogenesis. Likewise, atelectasis or cellular exudate or edema will obliterate the air spaces and cast the same roentgen

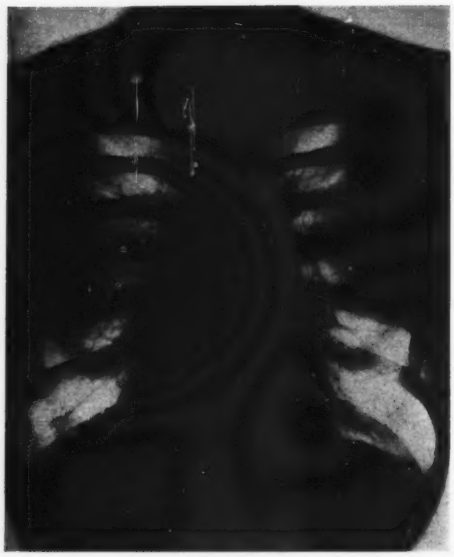


Fig. 2. An average normal adult chest with a small insert on the right to indicate the relative size of a secondary lobule, which, according to Miller, measures 1.5 to 2.5 cm. or more in diameter and contains from 50 to 250 primary lobules.

shadow but have an entirely different pathologic appearance and origin. The pathologist may describe the destruction of the bronchial walls or their air sacs by destructive processes, or demonstrate an increase in their thickness or density by the formation of fibrous tissue, but the differentiation between these two processes within a small group of anatomic units as portrayed on a roentgen film would be impossible by the roentgenologist, if only the small localized lesion is considered.

(*c*) The pathologic reactions within the arteries, the veins and their capillaries.

Again the pathologist may describe a stasis of the flow within the capillaries of a necropsy specimen which upon the roentgen film of a clinical patient will cast a shadow similar to that of a cellular exudate within the bronchioles and their air sacs or a shadow similar to an edema of these structures. Increased flow within the capillaries must exist but has little roentgen consideration. Occlusion of a nutrient artery may take place and produce a necrosis of the anatomic units preceded by the usual inflammatory changes. Or again, the capillaries may be occluded by tumor cells, with the subsequent formation of a metastatic nodule. There may be destruction of the vascular walls by acute infections or an increase in the supportive framework by more chronic inflammatory process. I wish to point out that few of these pathologic processes taking place within the vascular system of the anatomic units, can be differentiated from certain pathologic reactions in the bronchioles and air sacs, where the air content is completely obliterated, if only a small group of anatomic units are considered and if no consideration is given to the structural changes in the rest of the chest.

(*d*) Pathologic reactions within the lymphatic system. In the pathologic processes involving the lymphatics, the following conditions may occur:

1. The lymph channels may become distended or they may be compressed by adjacent disease.
2. The walls of the lymphatic channels may be caught in the pathologic process and destroyed, or in the more chronic conditions the walls may be thickened with definite fibrosis.
3. The flow of lymph may be blocked by cells or débris.
4. Nodes of lymphoid tissue are not plentiful within the anatomic units, but those present may have acute inflammatory reactions or chronic fibrotic reactions.

When such pathologic reactions within the lymphatic system of the anatomic units reach sufficient proportions as to interfere with the air content

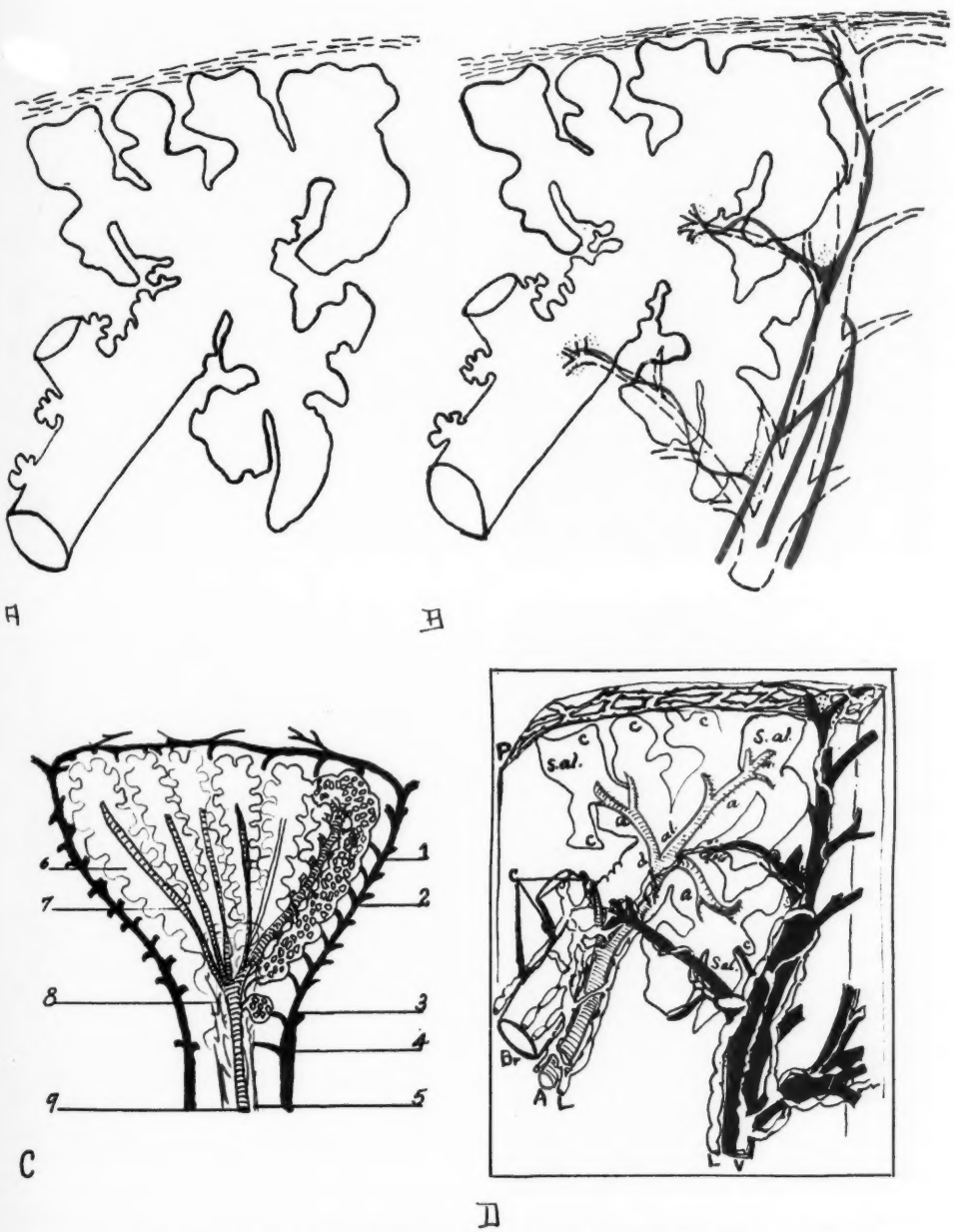
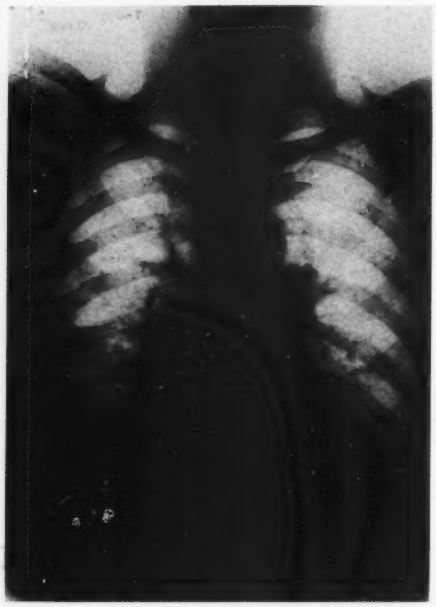
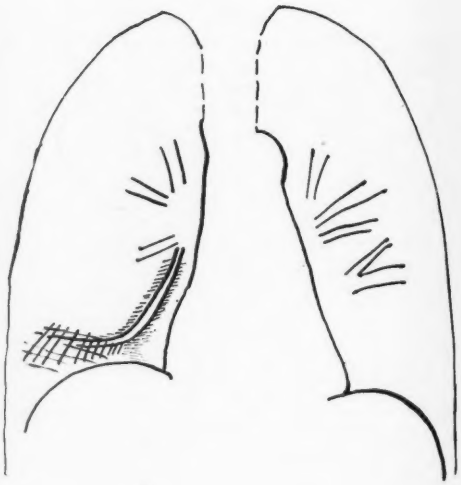


Fig. 3. Pen sketches, *A*, *B*, and *D*, are from the works of William Snow Miller and *C*, from Sauerbruch. Figures *A*, *B*, and *C* illustrate the three systems of the primary lobule; *A*, the respiratory bronchus and the air sacs, *B*, the lymphatics, and *C*, the vascular system. Figure *D* illustrates the three systems combined to form the primary lobule.





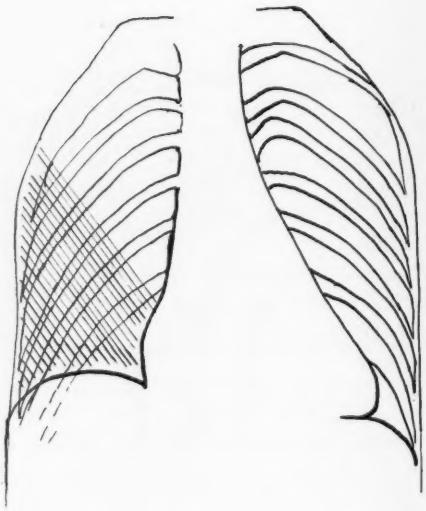
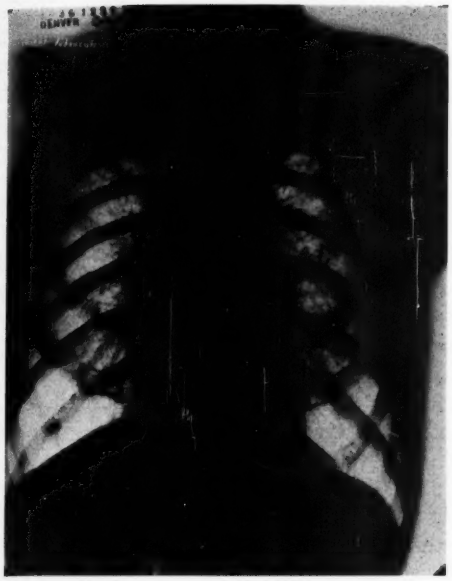
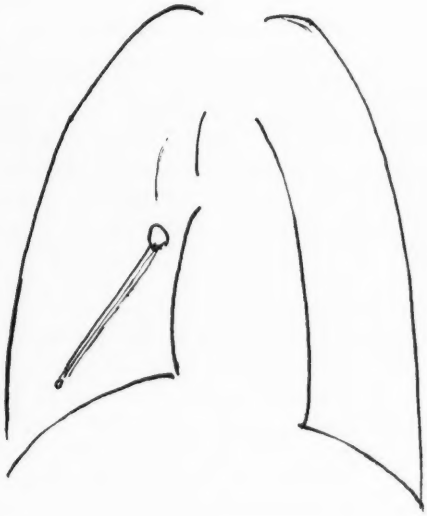


Fig. 4 (*above*). Pneumonia of the right base with involvement of the bronchus leading to the right lung root and an associated involvement of other bronchi of either lung root, illustrating a disease primarily of the ventilating system; but the diagnosis is not made entirely by the changes in the primary and secondary lobules.

Fig. 5 (*below*). Atelectasis of the right base involving especially the air sacs of the ventilating systems with a diagnosis made by the changes in other anatomical structures, as the sloping ribs and the high diaphragms.





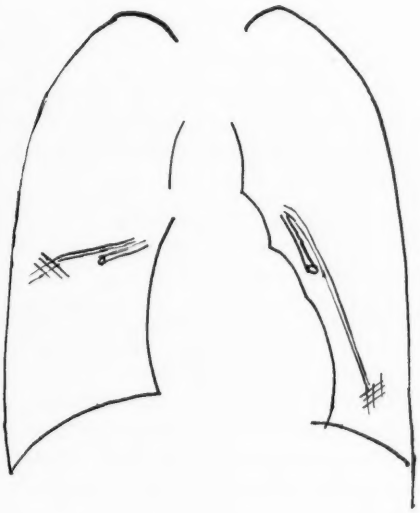


Fig. 6 (*above*). Pulmonary tuberculosis with an area of calcification in the right base and changes in the lymphatics extending along the arteries and bronchi to the lymphatic nodes in the lower portion of the right lung root. Here the disease involves primarily the lymphatic system, and only secondarily the ventilating system, and to a still less extent the circulating system.

Fig. 7 (*below*). Disease of the circulating system without anatomical changes demonstrated in the ventilating or lymphatic systems. The disturbance of the air content of the secondary lobules in the bases cannot be classified without a study of other anatomical changes, especially those of the heart.

of the adjacent air sacs, and when a sufficient number of units are involved, the reactions may be portrayed upon the roentgen film. The differential diagnosis of any one reaction, causing a disturbance of the air content from pathologic reactions within the ventilating system or circulatory system, requires more than the study of the anatomic units comprising a few secondary lobules.

(*e*) The reactions within the connective tissue framework supporting the bronchioles and the air sacs, the arteries, veins and their capillaries, and the lymphatic system may either undergo acute inflammatory changes or chronic fibrosis.

A discussion of their roentgen portrayal would be similar to that of the lymphatic system.

III. Classification.

It is evident from the foregoing brief description that the pathologic reactions within the anatomic units may be divided into those involving:

The ventilating system.
The vascular system.
The lymphatic system.

The reactions of the connective tissues or the supportive framework of the systems are secondary to the pathologic reactions within the ventilating, the vascular, or the lymphatic system. As just mentioned, the pathologist describes many reactions which are quite different in both appearance and origin, but as portrayed upon the roentgen film many of these reactions will cast the same type of shadow. The roentgenologist in considering a small group of anatomic units as one or two secondary lobules, may be able to differentiate a disease of the bronchioles and air sacs as in emphysema from an occlusion of the air sacs as in atelectasis or pneumonia, but when considering only one or two such secondary lobules, he could not differentiate atelectasis from pneumonia. For the latter differentiation he must turn to the structural changes in other portions of the lungs, the mediastinum and its structure, or the chest wall. Again in the stasis of flow within the capillaries, as in cardiac failure, a certain group of anatomic units might have the same appearance as a similar group of units in bronchopneumonia and only by an analysis of the heart outline and the changes in other portions of the lungs could one differentiate between the two. In other words, there are only a few pathologic reactions within the anatomic units of the lung which are distinctive or portrayed in a distinctive manner upon the roentgen film. The diseases involving the anatomic units do permit themselves to be classified into those primarily of the ventilating system, the vascular system, or the lymphatic system. The differential diagnosis is most frequently made by a study of the structural changes in the rest of the bronchial system when the bronchioles and air sacs are involved. In diseases of the vascular system with stasis of flow in the capillaries, the differential diagnosis is made by a study of the heart and great vessels, the location of the shadows, and the anatomic appearance of the rest of the chest. Again, the diseases primarily of the lymphatic system are differentiated from those of the ventilating, or vascular system by a study of the reactions within the lymph nodes along the major arteries and bronchi, or of those nodes at the lung roots or in the mediastinum. The attempt should always be made to differentiate and classify the diseases of the lungs into those of the ventilating system, the vascular system, and the lymphatic system. This should be done by a study of the structural changes, whether in the anatomic units or the other portions of the chest.

IV. The Diagnosis.

The diagnosis of chest diseases and especially those involving the parenchyma or the anatomic units of the lungs is based upon certain general considerations.

In a given patient with clinical manifestations of disease of the lungs, there will also be roentgen evidence of the disease. A patient with a typical clinical syndrome will usually have a typical roentgenographic syndrome.

The structural changes of the roentgenographic syndrome are portrayed chiefly by their disturbance of the normal position or relationship and the relative amount of the air content of the lungs.

The study of this air content of the anatomic units and particularly of the structural changes throughout the chest is the basis for the differential diagnosis.

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(4) Idem: Reference Handbook of the Medical Sciences, 1916, **6,** 89.

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DERMATOROENTGEN THERAPY

SHOULD THE COMMON DERMATOSES BE TREATED WITH FILTERED OR UNFILTERED RAYS?

By C. K. HASLEY, M.D., *Detroit, Michigan*

THE present status of dermatoroentgen therapy is in a state of flux. There has been no unanimity of opinion regarding the indications for the use of filtered and unfiltered rays. Many dermatologists employ unfiltered irradiation almost to the exclusion of filtered radiation. In our opinion, unfiltered rays are being used too extensively and too thoughtlessly. Unfiltered radiation is not always desirable even when little or no penetration is required to effect a cure. It is true, small doses do not provoke immediate damage, but the accumulative effect of fractional unfiltered doses is prone to produce a chronic roentgen dermatitis which may be serious in later years. Every physician who uses the roentgen ray for therapeutic measures should not only be thoroughly acquainted with both its possibilities and its limitations, but should attempt to prevent all detrimental post-radiation sequelæ.

To-day, our concept of skin tolerance and skin recovery is vastly different from what it was a decade or two ago. Formerly, the erythema dose (S.E.D.), with its many sources of error, was regarded as the absolute tolerance dose and hence the maximum dose of safety. To-day, when the disease process warrants extreme therapy, many erythema doses are given, as, for example, in treating malignancies of the skin and deeper tissues. This is done without fear of permanent damage to the skin. The technics commonly employed for multiple erythema dose treatments are: The Pfahler saturation method, the Coutard protracted fractionated method, and Holfelder's combination of the above two types of treatment.

Consequently, with the changed concept of skin tolerance it is *à propos* to ask again, what kind of rays are best suited for the treatment of common dermatoses? The answer is a difficult one. There are multitudes of variable factors which enter into a safe dermatoroentgen dose. If only one factor is changed at a time, the possibilities for dose variation assume geometric proportions. For example, the quality (wave length) of a skin dose may be changed by the potential. The quantity may be changed by the filters, by the time, by the milliamperage, by the distance, by the size of the field, etc. If the answer to the above question assumes any degree of finality, it presupposes the proper interpretation of all the experimental work in the biophysical, biochemical, and biological action of rays on living tissue. With such a multiplicity of variable factors, it is quite easy to understand why the empirical dermatoroentgen dose has been passed on and on, and it is also easy to understand why a permanent skin damage has not been done, as the total dose has not exceeded the skin recovery dose.

But, to-day, the chances for over-exposure by the divided and fractionated method are greater than ever before as the field of usefulness of irradiation therapy is greater. It is now being used in treating many diseases of infancy, childhood, and adolescence such as infections, allergy, and dermatoses. Consequently, it is necessary to exercise greater precaution to keep the accumulative factor of x-ray well below the skin tolerance.

It will be impossible to present within a limited discussion more than a few of the diversified factors which enter into a dermatoroentgen dose. The scope of that field is entirely too extensive for a discussion of this kind, but it is possible to point out some of the experimental work which has recently been done which will support the contention that unfiltered rays are being used too extensively in the treatment of common dermatoses.

Three major reasons will be advanced to support the contention that filtered rays are indicated in preference to the unfiltered ones.

1. The skin recovery following the Coutard method.
2. The response of inflammatory conditions to small filtered roentgen doses.
3. The radiobiological selectivity.

I. SKIN RECOVERY FOLLOWING THE COUTARD METHOD

In 1928 Coutard described and developed his technic. It was worked out in an attempt to imitate, as nearly as possible, the continued radium application as employed by Regaud and Nogier. The selective action of small amounts of radium employed for a long time had been noted by Regaud in treating malignant tumors. Consequently, Coutard substituted the short, penetrating x-ray in place of the radium, which necessitated the use of heavy filters and the administration of fractionated x-ray at low milliamperage. A severe skin reaction resulted similar to that produced by the Regaud radium method. Coutard distinguished between two forms of skin reaction, one, a radio-epithelite, and the other a radio-epidermite, the former being observed 14 days and the latter 28 days after the beginning of treatment. Dermatologists were rather reluctant to adopt this form of treatment for malignancies of the skin as they were interested in skin recovery and feared that permanent post-radiation sequelæ might be extremely distressing. But now the Coutard method has been used long enough so that an effective volume of data has been collected on skin recovery and skin repair. The epidermolysis which follows the Coutard protracted fractionated treatment produces from a partial to a complete destruction of the epidermal layers of the skin, leaving, however, a dermal layer with its vascular and connective tissue elements relatively intact. Epidermal regeneration occurs through the growth of the basal layer at the edge of the treated areas and by islands of epithelium which remain in the hair follicles. A soft pliable skin results. The changes in the cutis according to Schreus and many others, show little or no tendency to produce hard indurated fibrous tissue, and, on recovery, relatively little change is noted in the vascular system of the cutis. It is in these respects that the cutis presents a markedly different histopathologic picture than that found following the use of repeated roentgen-ray treatments with erythema or sub-erythema doses The latter type of treatment may result in a chronic radiodermatitis with marked change in the connective tissue and vascular system of the cutis. Clinically, this change can be detected by evidence of atrophy and induration. The very fact that there is better skin recovery following the Coutard technic than there is following the divided erythema or sub-erythema doses without filters, forms one of the strong arguments for the use of filters. Likewise, it forms a strong argument for the use of higher voltage and more filtration, as it is by this method that a homogeneous or a monochromatic type of ray may be developed and used.

II. RESPONSE OF INFLAMMATORY CONDITIONS TO SMALL FILTERED DOSES

The changes effected in inflammatory tissue by filtered roentgen rays may be mentioned as one of the indications for the use of filtered radiation in treating the common dermatoses. A review of the literature shows that metallic filters are employed as a common procedure by the radiologist in treating inflammatory diseases. Only one reference, Gaston Daniel,[1] was found with a technic employing 1 cm. of leather in the place of a metallic filter. This form of treatment was advocated for paronychia and furunculosis. Daniel employed a low kilovoltage of from 24 to 28 kv. with 1 mm. of aluminum filter and a dose of from 10 to 60 r for most of the inflammatory conditions. In this respect he is unlike many other therapists who employ a kilovoltage ranging from 80 to 200 kv. Daniel states

[1] Bull. et Mém. Soc. de Radiol. Méd. de France (Marseille Bull.), May, 1937.

that a small roentgen dose is imperative to the safety of the method. He notes improvement even when a small dose of 10 r is given, exceeding, he believes, the benefits of surgery and immunization. Daniel advocates the use of x-ray therapy in the treatment of acute and—think of it—hyperacute inflammatory conditions. In this particular respect he shares the opinion of the newer schools Many of the inflammatory conditions are definite indications for the use of irradiation therapy, and an inflammatory skin condition is no longer regarded as a contra-indication to the use of roentgen rays

V. G. Garshin, M. M. Bolshakova, and V. V. Orsinskaya[2] produced an aseptic inflammatory lesion experimentally by a subcutaneous injection of a 1–2 per cent suspension of infusorial earth into a rabbit's ear. When one skin erythema dose was given and repeated every four days for three times, no noticeable change was observed in the induced aseptic inflammatory granuloma, but a marked change was noticed when one-half S.E.D. was given every other day for six times. On section, the number of nuclei in the macrophage was greatly reduced over the control. Still greater change was observed when one-fourth S.E.D. was used. The giant cells and their nuclei were much smaller than their controls.

From their experiments these workers concluded that small fractional doses given at short intervals are more effective than larger doses at longer intervals. The clinical observation of many radiologists will support this contention. The late Dr. Manges, in an editorial entitled "Roentgen Therapy of Acute Inflammations and Infections,"[3] states: "The specific effect of roentgen radiation in infection may not yet be understood, but, empirically, under proper use and favorable circumstances, it is just as valuable as quinine was before the malarial parasite was discovered." The roentgen effect is due, in part at least, to the radiosusceptibility of the lymphocytes and the leukocytes. Only a small amount of irradiation therapy is needed to produce a destruction of the lymphocytes and in all probability an antibody is liberated on its destruction. Filtered doses permit the repetition of irradiation therapy frequently, if necessary, whereas the use of the unfiltered radion is limited.

III. THE RADIOBIOLOGICAL SELECTIVITY

For years, and notwithstanding the lack of experimental proof, some radiologists have felt, from the response of certain types of tumors to irradiation therapy, that the beneficial reaction was in part due to the selective quality of the waves. Some recent experimental observations tend to support this radiobiological theory. Henshaw and Francis, at the Fifth International Congress of Radiology, September, 1937, reported the results of experiments on seedlings, *Drosophila* eggs, yeasts, mouse sarcoma, etc., by using 30, 200, and 650 kv. The different radiations in like quantities and with like conditions produced different or unlike radiobiological effects. Consequently, they concluded that a differential action was due to the quality of radiation and that a selectivity of radiation does exist. They emphasized the point that the differential action cannot be neglected in considering the practical utility in radiation therapy.

These observations and conclusions are being cited to support the feeling that unfiltered rays are being employed too extensively, as the selectivity of the ray is increased by using a higher kilovoltage and more filters.

The trend in the treatment of infections as given by the radiologist is in the direction of greater filtration, and higher kilovoltage. But, unfortunately, it does not seem to apply to the method usually employed by the American dermatologist in treating inflammations of the skin. The dermatologists hold that for successful and safe roentgen treatment only the pathology should be treated. And it is true that in

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[2] State Roentgenologic, Radiologic, and Cancer Institute.

[3] Am. Jour. Roentgenol. and Rad. Ther., March, 1936.

certain dermatoses the pathology is extremely superficial, being confined largely to the upper layers of the corium and to the epidermis. But many of the dermatoses are the manifestations of constitutional diseases and the pathology is not confined entirely to the dermis. Filtered roentgen ray does penetrate beyond the skin pathology, and one should not overlook the fact that the benefits of irradiation therapy are both local and constitutional.

CONCLUSIONS

Filtered rays, in from one-eighth to one-fourth S.E.D., should be used in preference to the unfiltered rays in treating the inflammatory and common dermatoses. They can be repeated often if the diseased condition warrants it, with less hazard to the integrity of the skin. It is better to err on the side of filtered radiation than to err on the side of overdosing with unfiltered rays.

SKIN REACTIONS CAUSED BY 1,000 KILOVOLT AND 200 KILOVOLT RADIATIONS[1]

By ROBERT S. STONE, M.D., *San Francisco, Calif.*

From the Department of Surgery, Division of Roentgenology, University of California Medical School[2]

WHEN supervoltage radiation became available for treatments one of the advantages claimed for it was that much heavier doses could be administered through the skin without damage. Lauritsen (1) made some calculations of the energy absorbed in the surface when one roentgen was measured in beams of various qualities. These calculations suggested but did not state that more than double the number of roentgens, as measured in air, could be given with 1,000 kv. than with 200 kv. radiations. In our experience this is not true in the practice of roentgen therapy.

In the following discussion the term "high voltage" refers to the radiations from a 200 kv. General Electric X-P tube activated by a constant potential apparatus at 200 kv. and 15 ma., and filtered through the wall of the tube (0.2 mm. Cu equivalent) and 0.2 mm. Sn, 0.25 mm. Cu and 2 mm. Al, or 0.5 mm. Cu plus 1 mm. Al, as stated. "Supervoltage" refers to the radiations from the Sloan high frequency generator, operated at from 600 to 1,200 kv. and filtered through the tube wall of 1.5 mm. Cu plus 3 mm. steel, and then through 2 mm. Pb, 1 mm. Cu, and 1.5 mm. Al. When it first went into operation in 1934 this apparatus ran at 600 kv. Before the end of the year it was operating at 900 kv. In 1935 it was operating most of the time at 900 kv., but for two months 1,200 kv. were generated. During 1936 the operating voltage was 1,000 kv.

To compare accurately the results obtained by the use of these high voltage and supervoltage radiations it is necessary to vary no factors other than the quality of the radiation. The size of the fields, daily dosage, total dose, protraction in days and rate of giving (r per minute) must all be the same. We have kept them all as constant as possible except the r per minute. In 1934 the rate of giving for pelvic cases was 18.4 r per minute with the high voltage, and 31.6 r per minute for the supervoltage. Since then the first mentioned has been decreased to 12 because of increased filtration. At the same time the rate of giving the supervoltage radiations was altered to 25 r per minute because of changed emission. According to Holthusen (2), this would cause a change in the dose necessary to produce an erythema from 1,050 r at 12 r per minute to 850 r at 31 r per minute.

The roentgens are all recorded as if measured by a Victoreen condenser r meter and, unless otherwise stated, were measured in air. The measurements were made in the center of a beam 15 by 15 cm. in size with the thimble chamber against the end of the cone which was covered with celluloid or felt. At the beginning the measurements were actually made with an open air chamber on the supervoltage apparatus, and with a Fricke-Glasser dosimeter on the high voltage. Later they were correlated with the present Victoreen condenser r meter and all the readings converted to this standard. The symbol, "r," and the term, "roentgen," are used interchangeably for measurements made with the Victoreen condensor r meter in air whether in the 200 kv. or 1,000 kv. beams, even though it is recognized that such measurements of 1,000 kv. radiations may not be absolutely correct. *When the measurements refer to the ionizatio-*

[1] Presented before the Fifth International Congress of Radiology in Chicago, Sept. 13–17, 1937.

[2] This study has been aided by a grant from the Christine Breon Fund for Medical Research.

measured by the thimble chamber any place but in air the symbol r or the term, roentgen, are placed in quotations.

No systematic study has been made of the dose necessary to produce an erythema at one sitting. Our treatments are all given by the protracted method. As nearly as we can estimate, 800 r produced a definite erythema with the high voltage when given to a field 10 by 10 cm. in size at the rate of 12 r per minute. The difference between this and Holthusen's figure of 1,050 is probably caused by measuring the r in beams of different sizes. When the 800 r was given at the rate of 18.4 r per minute (due to lesser filtration) a more marked erythema resulted. With supervoltage radiations (1,000 kv.) 1,000 r to a field 15 by 15 cm. over the lower abdomen at the rate of 25 r per minute produced a very definite erythema and marked pigmentation. On the opposite side of the same patient's abdomen, 800 r of high voltage radiations, at the rate of 18.4 r per minute, produced in 35 days a more marked erythema with pigmentation; 50 days after the treatments no difference between the two sides could be detected. Eight hundred r of supervoltage radiations, at 25 r per minute, produced no change in fields measuring 10 by 10 cm. on the shoulder, abdomen, or hip.

Much more material is available for a comparison of the results of protracted treatment. The pelvis will be considered first. The routine in treating the pelvis is to use two fields anteriorly and two posteriorly, each 10 by 15 cm. in size. One anterior and one posterior field are treated one day, the other two fields the next day. Treatments are given daily except Sunday. With the use of the 200 kv. apparatus, 200 r per field per treatment—reaching a total of 2,000 r per field in 20 treatments during a period of 23 days—produced a definite erythema anteriorly with the formation of occasional vesicles, and a faint erythema posteriorly. When the filter was 0.5 mm. Cu and the rate of giving 18 r per minute, the reaction was slightly more severe than when the filter was 0.2 mm. Sn plus 0.25 mm. Cu and the rate 12 r per minute.

When the supervoltage was first used, 316 r per treatment, totaling 3,160 r per field, were given at the intensity of 31.6 r per minute. This produced a reaction considerably greater than that from the high voltage. Some of the reactions were so severe that treatments had to be stopped before completion, and the late results are now known to be too intense. In time it was found that 250 r per field per treatment, to a total of 2,500 r given at the rate of 25 r per minute, gave almost the same reaction as that obtained by the use of the high voltage, with the exception that it was about one week slower in reaching its peak, and that, while the pigmentation was about the same, there was less tendency to the formation of vesicles. The skin remained drier throughout.

On a few patients, one field on each surface was treated with supervoltage and the other with high voltage. In some, the supervoltage was given to the same side of the pelvis both anteriorly and posteriorly, and in others the opposing fields were treated with the differing qualities. In all these cases the fields treated with the 200 kv. radiations showed a slightly more marked erythema, but those treated with the 1,000 kv. radiations showed a more uniform reaction over the whole field. The pigmentation seen later was about equal for the two types of radiation.

From the preceding discussion, it appears that 200 r, air measure, of 200 kv. radiations given in 23 days elapsed time produces approximately the same reaction of the skin over the pelvis as 2,500 r, air measure of 1,000 kv. radiations. Lauritsen (1) calculated the number of theoretical roentgens required to cause the absorption of the same number of ergs per square centimeter of a surface layer of water 1 mm. thick at different monochromatic equivalent voltages. From his curve it can be seen that 525 r and 1,100 r delivered by 100 kv. radiations (200 kv. peak?) and 500 kv. radiations (1,000 kv. peak?), respectively, give the same num-

ber of ergs absorbed. This is an increase of over 100 per cent, whereas the present studies show an increase of only 25 per cent for supervoltage. We have not found a complete explanation of this discrepancy. The amount of back-scatter, the exit dose, the method of measuring roentgens, the rate or recovery of the skin, the value of the monochromatic equivalent voltage, and the rate of administration must all be considered.

The amount of back-scatter to the surface from a particular beam of radiation is controlled by the size of the field. For the field 10 by 15 cm. in size, this back-scatter, as measured by the Victoreen condenser r meter, is 35 per cent for the 200 kv. and 10 per cent for the 1,000 kv. radiations. The 2,000 r air measure of 200 kv. radiations, therefore, equals 2,700 "r" on the surface, and the 2,500 r equals 2,750 "r."

It was shown by Stone and Aebersold (3) that, in the case of supervoltage radiations, the exit dose becomes of appreciable size. When using 1,000 kv., 80 cm., target-skin distance and a field measuring 10 by 15 cm. it is approximately 20 per cent of the surface dose after traversing a section 20 cm. thick. With 200 kv., the other conditions being the same, the exit dose is only 10 per cent. Thus to the total applied skin dose in a cross-fire technic we have to add the exit dose, 550 "r" for the supervoltage and 270 "r" for the high voltage. Adding these exit doses, which, of course, include scattering, it is seen that each surface receives 2,970 "r" from the 200 kv. apparatus, and 3,300 "r" from the 1,000 kv. apparatus.

We are not prepared to discuss the measurement of the roentgen of 1,000 kv. radiations by the thimble chamber. We can say that with the thimble chamber which we used a slightly larger number of roentgens (about 10 per cent) was required than with 200 kv. radiation to produce the same effects on small biological objects. Thus to have the same biological effect the reading of the r meter needed to be 10 per cent more for 1,000 kv. than for 200 kv. radiations. If 10 per cent is subtracted from 3,300, we get 3,000 "r" as the surface dose from 1,000 kv. radiations, in comparison with 2,970 "r" from 200 kv. radiations.

The effect of the rate of recovery of the skin during protracted treatments is very difficult to measure or estimate. As was mentioned above, it takes a few days longer for an erythema, produced by a single exposure, to appear after 1,000 kv. radiations than after 200 kv. radiations. On the basis of previous experience with lower voltages it would seem that the recovery from 1,000 kv. radiations would be slower. With protracted treatments a greater accumulative effect could be assumed to result from the slower recovery.

The monochromatic equivalent kilovoltage is one way of stating the quality of the beam of x-rays. It gives the average energy of the photons in the beam but does not describe the distribution of their energies. This fact makes it extremely difficult to apply to practice in connection with heterogeneous beams of radiation, the information obtained from calculations based on an absorption of pure monochromatic radiation. The difference in the erythema dose for the two heterogeneous beams of radiation being considered would not be so great as that calculated for pure monochromatic beams of 100 and 500 kv.

The effect of the rate of administration of radiation (the r per minute intensity) on the production of erythema is at the present time the subject of considerable controversy. It seems certain, however, that there is some effect and that it takes a larger dose to produce an erythema if that rate is low and the time taken to administer it longer than if it is high and the time shorter. If this is true it would have taken more than 2,500 r to produce the same results with the supervoltage if the rate had been 12 r per minute instead of 25.

Whatever the explanation may be, we are forced to conclude that, in protracted therapy to the pelvis as described, the number of roentgens as measured in air with the Victoreen condenser r meter can be only about 25 per cent greater for 1,000

kv. radiations than for 200 kv. radiations. When back-scatter, the "exit dose," and the equivalent dose as measured by small biological test objects are taken into consideration the number of "roentgens" as measured on the skin is almost the same for supervoltage as for high voltage radiations when the same reaction is produced.

The practical roentgen therapist is interested in knowing whether, for the same reaction of the skin, a greater amount of energy can be delivered into the body and absorbed there by the use of the one radiation or the other. From Lauritsen's calculations on the theoretical roentgen and monochromatic equivalent voltage, it is found that the total amount of energy in the beam for the same absorption of energy per square centimeter of the surface increases rapidly with the equivalent voltage. Thus it would seem that even though the effect on the surface is the same for the two voltages, the actual amount of energy delivered into the patient would be much greater for the supervoltage. In therapy, however, one is concerned not with the energy delivered, but with the energy absorbed.

If the ionizing effect in a thimble chamber at various depths is accepted as an index of the amount of energy absorbed, then that amount is greater under some conditions for high voltage than for supervoltage radiations. Mayneord and Roberts (4) have shown, for radiations up to 370 kv., and Stone and Aebersold (3) for radiations up to 1,000 kv., that the dose at various depths up to 8 cm. is somewhat greater at lower voltages than at higher. The variations in this dose depend on the size of the field and the focal skin distance as well as on the kilovoltage. When cross-fire technic is used, the greater exit dose with supervoltage also decreases the total dose that can be delivered to the center of sections of finite thickness.

In the Section on Physics of this Congress, Aebersold and Chaffee (5) are reporting measurements made on sections of finite thickness with various sizes of fields using direct cross-fire. They have found that using a field 50 cm.^{2} in size, 80 cm. target-skin distance and voltage factors as described above, equal or greater doses can be delivered to the center of solid sections up to 12 cm. thick, for the same surface "r" doses, by 200 kv. than by 1,000 kv. radiations. For fields 100 cm.^{2} in size this holds true up to 14 cm.^{2}, for 225 cm.^{2} up to 16 cm., and for 400 cm.^{2} up to 18 cm.

It is thus obvious that, when considering sections of definite thickness, more ionization is produced in the center of thin sections when using 200 kv. than when using 1,000 kv. radiations. If the effect on tissues depends on ionization alone, and if the thimble chamber gives a fair estimate of that ionization, then 200 kv. radiations may be superior to 1,000 kv. radiations in some situations.

It is an all too common belief that the effect on the skin is the only factor limiting the amount of radiation that can be given. When treating pelves with either 200 kv. or 1,000 kv. radiations we have frequently found that we have had to stop treatments because of a severe diarrhea, or that, long after treatments have been completed, the patients have continued to complain of pain in the abdomen which we believe to be the result of injury to the intestines. Some months after the skin of the neck has completely recovered we have found patients who had been treated for lesions of the throat still suffering from severe edema of the mucosal and submucosal tissues. Treatments to the chest which have caused no changes in the skin have given rise to severe reactions in the lungs. All of these complications have been obtained as frequently by 200 kv. as by 1,000 kv. radiations when the 200 kv. radiations were delivered from a distance of 80 cm. Hence, it is my belief that, with a proper use of 200 kv. radiations, as much effect can be produced in the interior of all but the thickest patients as their tissues will stand. Progress is to be made not by increasing voltage but by changing such factors as protraction and the r per minute intensities. Supervoltage is useful for producing high intensities at long target-skin distances, but one must not confuse the effects of increased target-

skin distances with those of increased voltage.

Some of the doses actually administered are of interest and value to those contemplating supervoltage therapy. In nearly all regions of the body we treat opposing fields on alternate days, and have used 20 days of treatment in from 20 to 25 days elapsed time as our mean. In general, it may be stated that the immediate skin reaction from 1,000 kv. radiation tends to be drier for the same degree of pigmentation as seen at the end of two months than that produced by 200 kv. radiation.

Tables I and II show the results in a few patients treated over the pelvis and selected because the records of the reaction of the skin at various times were sufficiently complete. They show that those treated with an average of 300 r per port per treatment, to a total of 3,000 roentgens per port in from 20 to 25 days elapsed time, had a higher percentage of severe immediate reactions and all of the late severe changes. We have treated a few patients with 400 and more roentgens per port per treatment, reaching totals of 4,000 roentgens per port in from 20 to 25 days. All of these have had very severe primary reactions that were slow to heal.

Table III shows the mucosal reactions as estimated by the severity of the diarrhea produced. It is plain that marked diarrhea is frequently caused by the smaller doses which gave the less severe skin reactions. It is our belief that in treating pelves there is no justification for producing severe skin or mucosal reactions. The results do not justify the immediate suffering nor the threat of late changes. All of those treated with more than 300 r per port per treatment developed very severe diarrhea.

In the treatment of lesions of the throat we have frequently prolonged the treatment beyond the 20 sittings and have varied the daily dose because of the general reaction. We have also found great variation in the skin and mucosal reactions of individual patients. We have frequently added a posterior port to the two lateral ports without noticeably increasing the skin reaction. In general we have given an average of 265 r per port to opposite ports and treated them on alternate days to an average total of 2,800 r per port. Of 24 patients so treated only eight had a severe epidermitis, whereas 20 had severe epithelitis. The period of observation has been too short to tell what the late changes in the skin will be, but we know that many patients have developed marked edema of the throat. We feel that we are limited by the mucosal changes more than by the skin changes, but this same condition holds true for 200 kv. radiations if heavily filtered and given with 80 cm. target-skin distance. We have used fields 10 by 10 cm. in size, or larger, in most cases.

Eight patients with lesions of the breast, not operated on, have been treated by the tangential method using two oblique fields 10 by 20 cm. or larger. In these cases an average of 2,500 r per port in 23 days

TABLE I—PELVIS—EARLY SKIN REACTIONS
1,000 KILOVOLTS

Daily Dose per Port	Total Dose per Port	Type of Reactions			
		None	First Degree	Dry Peeling	Second Degree
300	3,000	0	3	8	6
250	2,500	2	4	13	4

TABLE II—PELVIS—LATE SKIN REACTIONS
1,000 KILOVOLTS

Daily Dose per Port	Total Dose per Port	Type of Reaction			
		Recovery	Dry Pigmentation	Telangiectasis	"Leather" Skin
300	3,000	4	0	2	4
250	2,500	6	6	0	0

TABLE III—PELVIS—MUCOSAL REACTIONS

Daily Dose per Port	Total Dose per Port	Degree of Diarrhea			
		None	Mild	Moderate	Severe
300	3,000	1	0	9	2
250	2,500	3	3	6	4

elapsed time produced a severe epidermitis from which the skin recovered in the second month.

A sufficient number of examples have now been given to show that the doses given and the reactions which resulted do not differ greatly whether 200 kv. or 1,000 kv. radiations are used. While it is too early to speak of end-results, the number of patients already dead convinces us that no great improvement over the results obtained by 200 kv. radiation with similar protraction can possibly result.

In the foregoing discussions no account is taken of any as yet unproved wave length effects.

SUMMARY

1. A comparison is made between the effects on the skin obtained by the use of radiations from a 200 kv. constant potential apparatus and from a 1,000 kv. Sloan type generator.

2. It is shown that, while an increase of 25 per cent in the number of roentgens measured in air can be given with the 1,000 kv. radiations, the increase in the dose as measured on the skin, with the addition of the exit dose, is negligible.

3. The amount of energy absorbed in the depths as measured by a thimble chamber ionization meter is not greater in many thin parts for 1,000 kv. than for 200 kv. radiations.

4. The limiting factor in many instances is not the skin reaction but the reaction of the mucosa and other deep structures, whether 1,000 kv. or properly used 200 kv. radiations are employed.

5. The real value of 1,000 kv. radiations lies in the treatment of very thick patients, or when very small fields can be used.

6. Progress in radiation therapy is more likely to be made by varying factors other than kilovoltage.

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TUMORS INVOLVING THE SKELETON

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TUMORS of bone present features of great clinical, roentgen diagnostic, and radiotherapeutic interest. The addition of new case records to existing compilations is desirable, particularly of neoplasms with unusual features. The presentation of the following group, therefore, seems appropriate in this issue of RADIOLOGY, especially as all of these cases were seen in the Department of which Dr. Rollin H. Stevens is the Director.

There exists in the medical literature a controversy concerning metastatic tumors developing from apparently benign primary tumors of the thyroid gland. The subject was reviewed critically by Simpson, who came to the conclusion that, on most careful analysis, all these cases should be regarded as metastases of a primary very small carcinoma of the thyroid gland, imitating types of benign tumors of the thyroid to such an extent that they are most easily confused with non-malignant neoplasms. Such a case is reported herewith.

CASE REPORT

The clinical history available at this time, 16 years after the patient's death, is most incomplete, but a careful autopsy report is available and also histologic sections.

The patient was a white male, 80 years of age. About four years prior to his death he contracted pneumonia and for some prolonged time afterward was afflicted with an unpleasant cough and expectoration. For several weeks his sputum contained numerous tubercle bacilli which, however, finally disappeared rather rapidly with all clinical manifestations of any type of pulmonary disease. In April, 1921, his right clavicle fractured without any known provocation. The x-ray report at that time stated that a fracture through the middle third of this clavicle was surrounded by an area of diminished density of the bone, believed to represent a bone cyst. This fracture healed incompletely, with considerable delay. In the Fall of that year paralysis developed in the lower half of the body, and in roentgenograms obtained under very unsatisfactory circumstances one thought to discover a collapse of the third dorsal vertebral body. The patient subsequently succumbed to a pneumonia.

From the autopsy report by Dr. C. I. Owen, Director of the Laboratories of The Grace Hospital, we quote:

"There is a small visible and palpable enlargement in the outer third of the right clavicle, hard and bony to the touch. There is no visible nor palpable enlargement of the thyroid gland. There are no other external markings of importance.

"Right Lung.—Extensive pleural adhesions over this entire lung were present. The lymph nodes at the bifurcation of the trachea were somewhat enlarged, markedly anthracotic, and upon incision into some of them, there were found caseated and partially calcified areas. A bronchopneumonia prevailed throughout the lower lobe, which was somewhat firmer on palpation, had a much redder appearance, and from the cut surface of which numerous small droplets of pus were expressed. On section of the upper lobe localized bronchopneumonic areas were found, from which also small droplets of pus exuded. The middle lobe did not exhibit evidence of disease.

"In the upper mediastinum there was a mass of aberrant thyroid tissue about $9 \times 7 \times 6$ cm. in size. Its gross characteristics were those of a colloid adenoma. This mass had pushed the trachea over to the right so that a semicircular indentation had occurred. It was not connected with the thyroid gland.

"Thyroid Gland.—The right lobe, isthmus, and lower portion of the left lobe contained normal thyroid tissue. The upper portion of the left lobe over an area of about 2.5 cm. was adenomatous in character, not definitely malignant. In the outer third of the right clavicle there was an irregular enlargement about one-half again the normal diameter. At this point a fracture occurred on simple manipulation. The bone at this point consisted of a thin shell from 1 to 2 mm. thick. The medullary portion of the bone throughout contained a

colloid type of material not unlike that found in the left lobe of the thyroid gland and in the aberrant mass present in the mediastinum.

"In a portion of the third thoracic vertebra there was an area of colloid material similar to that found in the clavicle, having replaced the bone and communicating with the spinal canal, the growth extending into and pressing on the spinal cord at this point. Chronic deforming spondylitis involved the fourth to sixth dorsal and several of the lumbar vertebræ.

"Histologic Findings.—Bronchopneumonia. Colloid adenoma of the thyroid gland (Fig. 10-*A*). Metastatic tumors, consisting of colloid adenoma, involved the mediastinum, the right clavicle, the third thoracic vertebra."

Otherwise, this autopsy revealed no evidence of anomalies or disease processes.

Correlating this autopsy report to those points of the patient's history recorded above, one feels inclined to conclude that several years before his death a pneumonic infection lead to the rupture of a caseated tracheobronchial lymph node which discharged its contents and subsequently healed without having produced a parenchymal dissemination of a tuberculous infection. Furthermore, metastases occurred in the mediastinum and skeletal segments from an adenoma of the thyroid gland. The pathologist was unable to find any evidence of carcinoma, either in the primary adenoma or the metastases. Clinically, no tumor of the thyroid ever was apparent. While offhand one would feel inclined to share Simpson's view referred to, this case might be cited in favor of the assumption that occasionally histologically benign tumors of the gland metastasize to distant organs.

In connection with this case of metastasizing adenoma of the thyroid we include in this report a résumé of the early history of a multiple myeloma which is quite interesting. We regret though that a complete review is impossible as this patient was seen only a few times in consultation. He died finally in another institution, and detailed information later on was refused us by this hospital. Seventeen months prior to the first consultation this patient, white male, age about 50 years, while camping in a Canadian cottage during a cold wintery night developed a swelling in the right cervical gland region with a sensation of a wry-neck. The soreness disappeared slowly, but the swelling of the glands persisted. The patient visited a well-known hospital but, dissatisfied, left their care. Subsequently, a pediatrician friend examined him and apparently regarded the glandular swelling very lightly, informing him that it would probably disappear without any particular treatment, though this resolution might require several months. One year after the onset of this swelling another physician was consulted. He resorted to treatment consisting of subcutaneous injections, which in all probability contained arsenic, iron, and strychnine. When no result was obtained, a biopsy was suggested and finally performed 15 months after the onset of the disease. The pathologic report submitted by a highly competent examiner was: "Lymphosarcoma of the reticular cell type." Later, the patient received extensive radiation therapy to neck, supraclavicular regions, both axillæ, mediastinum, spleen, and both groins. The effects of this treatment upon the lymphadenopathy in the neck were entirely negligible although unquestionably full erythema doses were applied under heavy filtration, from which the resulting tanning was quite apparent at the time he visited us.

In consultation we observed a rather hard adenoma in the thyroid just to the left of the midline. There was an extensive lymphadenopathy involving the cervical lymph nodes on the right side. These nodes were of hard consistency; the overlying skin, as mentioned, was quite tanned, and no hair was present. There was evidence of a former otitis media and mastoiditis, with partial sclerosis of the temporal bone and formation of a very large cell—demonstrated roentgenographically. Roentgenologic examination of the chest revealed a deviation of the trachea to the right at the upper thoracic aperture with a mild hourglass-shaped compression of the

trachea. This deviation was produced by a tumor in the thyroid region which showed irregular calcification. Otherwise, no evidence of disease was discovered on physical and roentgenological search.

Hematologic examination revealed a "moderate degenerative anemia of a hyperchromoligocythemic type," furthermore, a "regenerative shift of the neutrophiles with a low total count," and finally a "mild hyperbasophilia." After all medication had been discontinued for some time there remained in the hematologic picture a "mild secondary normocytic regenerative anemia" in the presence of a "normal total white count with moderate regenerative shift of the neutrophilic series." There was then a "persistent lymphocytopenia and mild eosinophilia." The impressions of the blood studies reported at this time were:

"At present the blood picture presents a mild irritative hyper-regenerative picture affecting the neutrophiles only. The causative factors still present seem to be not of a septic nature, since a hyper-eosinophilia was observed. The depression factor which influenced the hemoglobin and the red blood count levels seems to have been eliminated. As a whole, the picture has improved."

Clinically we could not readily subscribe to the histologic diagnosis of lymphosarcoma for the following reasons: The growth persisted for from 16 to 18 months without appreciable change. It was not influenced at all by radiation therapy. The presence of a tumor in the thyroid gland apparently had been entirely disregarded. Therefore, we suggested for diagnostic consideration the presence of either a malignant tumor in the thyroid gland or derivation therefrom, with metastases to cervical lymph nodes.

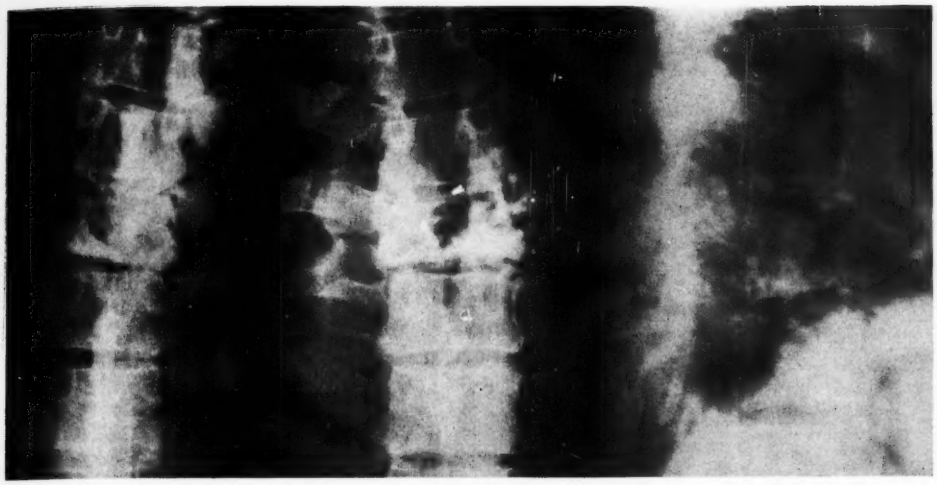
We communicated again with the pathologist who had submitted the original tissue diagnosis of lymphosarcoma of the reticular type and received the following information:

"The tumor presents the appearance of a diffusely infiltrating mass, having the general appearance of alveolar reticulum-cell sarcoma. However, the diagnosis of the small type cell of thyroid carcinoma may be considered in view of the fact that this type of tumor has often in the past been confused with sarcoma. I am unable to be positive in the matter, but feel certain that it is either a reticulum-cell sarcoma or a small-cell carcinoma of the thyroid."

Through the kind co-operation of this pathologist we obtained a stained tissue slide which was submitted to Dr. Broders, pathologist to the Mayo Clinic. He returned the diagnosis of plasma-cell myeloma. After this information had been submitted to the patient he never returned for any further consultation. We learned that he died approximately two years later, with the typical clinical manifestations of multiple myeloma.

It is apparent from this unfortunately very incomplete case record that this type of disease does not always follow the generally accepted course, that a clinical diagnosis may be extremely difficult, particularly if highly trained pathologists render such varying opinions. In this instance soft tissue manifestations—tumors—were the earliest signs of myeloma and lasted in rather stationary form from two to three years before generalized skeletal symptoms became apparent. The sudden onset of the observed swelling, the presence of a tumor in the thyroid gland, the familial disposition to thyroid disease, the lack of response of manifest tumor masses to radiation, the absence of any of the clinical and roentgenologic conditions, on which a diagnosis of multiple myeloma might have been based—all these facts could hardly lead to a diagnosis such as finally was established from histologic examination of a biopsy.

Geschickter and Copeland, in their book "Tumors of Bone," emphasize six conditions which, taken in pairs, triads, or collectively as a group, assume a diagnostic value of the first order, while in themselves they do not constitute conclusive evidence of multiple myeloma. They are (1) multiple involvement of the skeletal trunk in an adult, (2) pathologic fracture of a rib, (3) the excretion of Bence-Jones bodies, (4) characteristic backache with signs of early paraplegia, (5) an otherwise inex-



A 9-17-36 B 5-14-37 C 5-14-37

Fig. 1.

plicable anemia, and (6) chronic nephritis with nitrogen retention, low blood pressure, and high serum protein. To their collection we add two cases.

Case No. 37704. White male, aged 50. Thirteen years prior to admission he had suffered from a "renal infection." For five months previous to admission he noticed gradually increasing sensory and motor disturbances in his lower extremities—"did not know where his abnormally cold feet were; sensation of needles in his legs; loss of co-ordination of lower extremities; loss of motor power now extending to the lower ribs." He also complained much of lumbar back pain. He had been told by one physician that he was afflicted with a case of the very common lower back pain, and on this information took a number of chiropractic treatments.

On admission there was hyperesthesia extending from the feet to the umbilicus. Head and chest would perspire quite profusely down to the eighth dorsal segment, but the body was dry below this level. Reflexes were lost in lower limbs and abdomen; the left cremasteric reflex, however, was present. There was weakness and some spasticity of the lower extremities. Pulling the head forward caused pain in the midportion of the back. The spinal fluid was slightly xanthochromatic. A definite block was observed on jugular compression. Five cubic centimeters of ascending lipiodol were injected in the lumbar region for subsequent roentgenologic examination. Spinal fluid: globulin +; total protein, 85 mg. per 100 c.c.; two white blood cells per c.mm.; gold curve, negative; Eagle, Kline, Kahn tests, negative; 5,730,000 red blood cells; 11,800 white blood cells; 86 per cent polymorphonuclears; 14 per cent small lymphocytes.

Roentgenograms (Fig. 1-*A–C*) showed an obstruction of the spinal canal at the level of the eighth dorsal vertebra. There was involvement of the body and both pedicles of the seventh dorsal vertebra by a bone tumor, creating isolated areas of demineralization. There was considerable dilatation of the heart and aorta. No sign of pulmonary disease was discovered, and the humeri, lumbar spine, pelvis, and femora appeared to be normal. One of our associates, who originally reported the roentgen-ray evidence, felt that a neoplasm was present in the seventh dorsal vertebra, though he did not feel entirely certain that an inflammatory process could be ruled out definitely. In consultation we suggested the probability of a myeloma. A laminectomy was performed and "the

laminæ of the seventh and eighth dorsal vertebræ were found to be involved by tumorous tissue [Dr. E. S. Gurdjian]. These laminæ were removed and as much of the tvmor, which was pressing against the spinal cord, as was compatible with careful work, was resected."

Histologic Report.—The tissue is new-growth with a scanty, fibrous tissue stroma, trabecular in architecture. The parenchyma is composed of somewhat anaplastic plasma cells, which vary in size somewhat but average ten to fifteen μ. Some of them contain hyperchromatic nuclei and an occasional large prominent nucleolus is present. Some cells appear as small lymphocytes. There are many blood spaces and new blood vessels. (See Fig. 10-*B*.)

Diagnosis.—Plasma-cell myeloma (Dr. C. I. Owen). This patient expired nearly ten and one-half months after admission. Two months before his death no manifestations of myeloma could be discovered anywhere else in his skeleton. Radiation treatment to the involved vertebra was without any demonstrable effect. He grew weaker gradually and developed marked abdominal distention, with severe edema of his lower extremities, pain and sensory disturbances in the upper extremities. Bence-Jones bodies were not found in his urine even at repeated examinations, nor was there ever recorded any evidence of nephritis in his urine though no blood chemistry was done. An autopsy could not be secured.

The available observations on this patient thus revealed backache, with signs of early paraplegia, and a multilocular destructive process in the body and laminæ of the seventh dorsal vertebra, while all other evidence which might have supported a diagnosis of myeloma was missing. This suggested diagnosis was confirmed histologically. As far as we know, this patient did not develop grossly demonstrable myelomatous lesions anywhere else in his skeleton. His death resembled that of myocardial failure. Monostotic manifestations of myeloma are quite rare though some apparently have been observed.

Case No. 82888, in contrast, represented the text-book picture described by Geschickter and Copeland. The patient was a white male, aged 52, who complained three months prior to admission about rheumatic pains in the chest and back, improving under medical care. On the day of admission, while riding in a street car, his thigh suddenly flexed without apparent cause under considerable pain.

He had suffered from intestinal obstruction and peritonitis ten years previously. He harbored lipomas in the right lower abdominal wall, and on the anterior surface of the right thigh. Figures 2-*A* to 2-*D* show the appearance of the fractured right femoral shaft and its subsequent configuration during nearly one year. From the appearance of the bone, with a central area of destruction and adjacent osteosclerosing reaction, a neoplasm was suspected immediately but for a short time the possibility of metastasis from a tumor of the urinary tract or the thyroid gland was entertained. On further search of the skeleton, however, three weeks later other foci of bone tumors were found in ribs, lungs, and other skeletal segments, so that the diagnosis of multiple myeloma became quite apparent. Two characteristic views of skull and femur (Figs. 2-*E* and 2-*F*) illustrate the classical appearance of this widespread disease. Radiation therapy was without any effect. Bence-Jones bodies were found in the urine, together with albumin, about five months after admission and from then on till the patient's death. Gradually increasing anemia was observed. On a few occasions blood phosphorus was found to fluctuate between 3.7 and 4.4 milligrams per hundred cubic centimeters, while blood calcium fluctuated between 9 and 11.1 milligrams. Increasing calcification of the arterial system was observed during his stay in the hospital, which is also apparent in the last roentgenogram of the fractured femur (Fig. 2-*D*).

The patient succumbed to his disease twelve and one-half months following the original admission to the hospital.

A 5-15-31 B 6-6-31 C 7-20-31

E 4-20-32 D 4-20-32 F 5-30-32

Fig. 2.

From the autopsy report we merely state that a bronchopneumonia terminated his suffering. Foci of multiple myeloma were widely spread throughout the skeleton, and histologically were of the plasma-cell type (Fig. 10-*C*). There was a chronic nephritis, a pronounced arterio-

sclerosis, and myocarditis. As stated above, this case offered a text-book picture of this skeletal disease, and the only one of the diagnostic symptoms missing was an early paraplegia, though it should be remembered that not all evidence developed simultaneously.

Very occasionally we encounter widespread manifestations of skeletal invasion by neoplastic disease which might resemble in their roentgenographic appearance early signs of multiple myeloma, that is, small rounded, somewhat carelessly punched-out-appearing bone defects, associated with an indefinite osteoporosis and somewhat irregular appearing architecture of the cancellous bone. We had occasion to observe one such patient for whom the final diagnosis of chloroma was definitely established from a lesion located in a resected costal segment. This patient's history is given herewith.

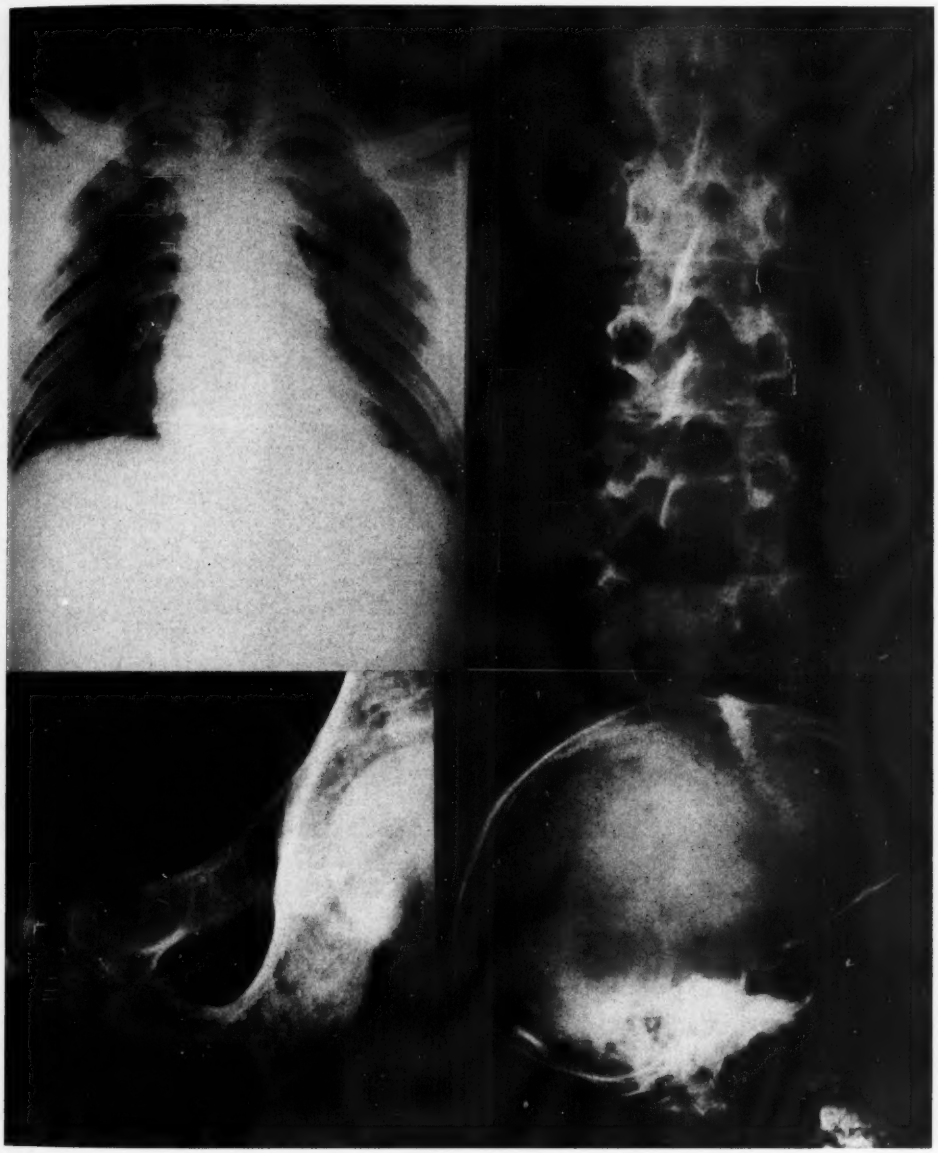
Case No. 95214. White male, aged 21 years. The early history, as it was given to us, sounds somewhat fantastic. While being baptized, at the age of nine months, his right leg was struck against the baptismal font. That night a temperature of 105 degrees developed, with apparent pain and tenderness in the injured extremity. Following an expectant treatment for two months he was operated at a hospital in Albany, N. Y., and much pus evacuated. We learned by correspondence with this institution that a diagnosis of cellulitis of the leg and thigh was made. Following a convalescence of three months he began to walk at the age of fourteen months, when a right-sided limp was observed. At the age of five years he was injured in an automobile accident and received severe lacerations to the anterior surface of the right thigh. He was then in a hospital, the name and place of which he cannot remember, for ten weeks. At the age of eight years he had measles and pneumonia. At fifteen, he had a dry cough and pain in his anterior chest, but physical and roentgen examinations at that time revealed no evidence of disease, particularly no sign of tuberculosis. For the past six or seven years he has had bleeding gums when biting apples or brushing his teeth.

In November, 1933, he complained of pain in the right side of his chest and epigastrium without cough or temperature. Since that time he had lost considerable weight. Later, distress developed in the right sacro-iliac region. By December the pain had become much worse and spread to his knees, hips, ankles, and fingers. It was quite intermittent in character. He was afflicted with marked anorexia and night sweats. The family physician, Dr. R. Q. DeTomasi, saw him first in January, 1934, with the complaints mentioned. Under the diagnosis of rheumatic fever he was hospitalized toward the end of January and treatment with salicylates was instituted. Within a week he felt much improved and went home. However, two days later his pain returned. It was most marked at this time in the sacro-iliac areas, and the right upper abdominal quadrant. It was so severe that he had to be readmitted to the hospital.

Physical Examination.—Weight approximately 90 pounds. Skin dry, eyes sunken, lips cracked and covered with dried blood from bleeding gums which were swollen and tender, especially along the dental margins. A chain of glands was felt in the posterior cervical region bilaterally. Small glands were palpated in either supraclavicular area; also the axillary nodes were slightly enlarged but not tender. On palpation considerable tenderness was elicited along the course of several ribs and on pressure over the costal arches, also under the left costal arch in the region of the spleen, which was palpable four fingers below the costal margin and two fingers from the midline. The liver was enlarged three fingers below the costal margin, less tender than the spleen. Both costal vertebral angles were quite tender. There were scars on the right hip and thigh. The right hip itself was extremely tender on palpation and motion. Otherwise, the physical examination revealed nothing of importance.

Laboratory Findings.—Hemoglobin varied from 32 to 62 per cent, with corresponding red counts of from 1,500,000 to 3,106,000 under the influence of repeated blood transfusions. The white count showed a relative lymphocytosis, occasionally up to 63 per cent, while the total count varied between 3,900 and 6,850 cells per cubic millimeter. No Bence-Jones bodies were found in the

A 2-22-34 B 3-31-34



C 2-22-34 D 4-10-34

Fig. 3.

urine, which was always negative for sugar and albumin except on three days of intense salicylate medication when a trace of sugar occurred. Occasionally hyaline and granular casts were observed in the urine.

From the x-ray studies we quote the following remarks:

"Bony structure throughout the thoracic cage and shoulder girdles appears somewhat irregular as if bone were extensively involved by a process producing a certain degree of osteoporosis with loose texture of cancellous bone and in certain parts small, ill-defined deficiencies, somewhat resembling small punched-out areas. Such a punched-out defect was found in the left seventh rib near the posterior axillary line. There was a severe left sacro-iliac arthritis and of a less pronounced degree on the right side. Peculiar osseous deficiencies, as mentioned, were also found throughout the pelvis, especially in the ischial and pubic rami; furthermore, in the proximal portions of the femora and lumbar spine."

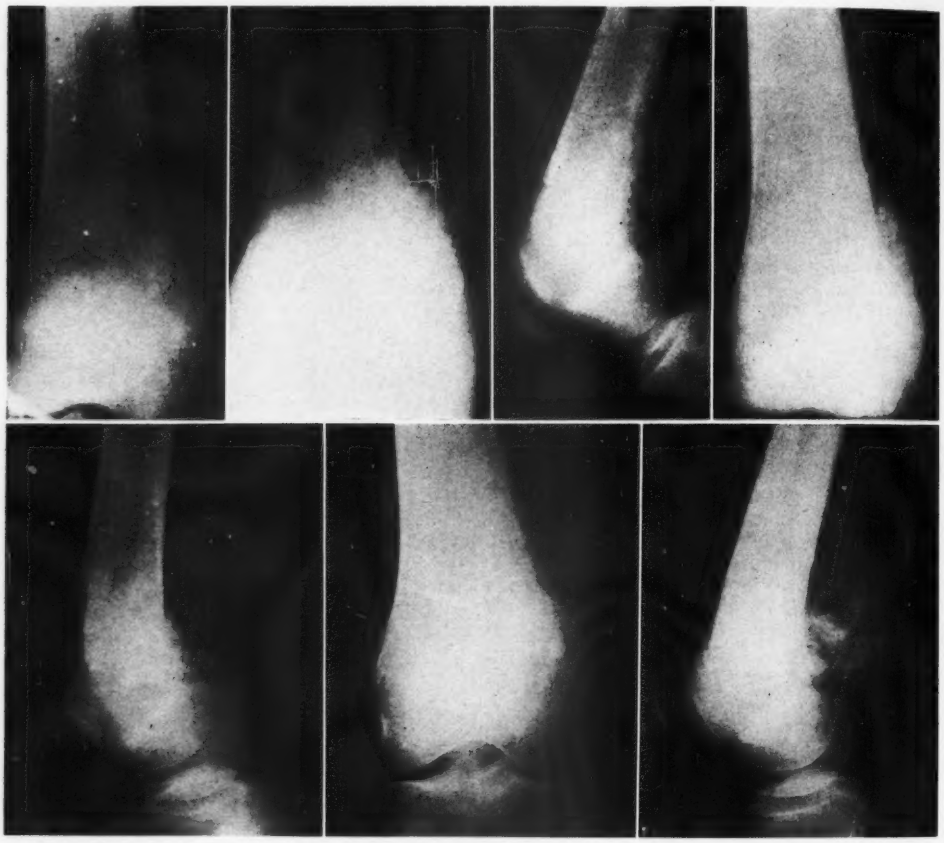


Fig. 4.

In April widespread similar foci were found in various bones of the facial skull and some also in the calvarium (Figs. 3-*A*—3-*D*).[1]

No radiation therapy was employed though a histologic diagnosis of chloroma (lymphoblastic type) was made by Dr.

[1] See also Dr. Shebesta's paper on mastoiditis in this issue.

C. I. Owen following resection of a costal segment in which a lesion was quite apparent roentgenographically (Fig. 10-*D*). This diagnosis had previously been suggested by Dr. Howard P. Doub, who had seen two similar patients. After the first transfusion spleen and liver decreased in size, pain and tenderness disappeared; after the second transfusion the gums assumed a healthy appearance, no longer bled, and the patient felt fairly comfortable with but occasional tenderness in chest, sternum, and clavicle. In this condition he left our institution and his family physician. A consultant called by the family expressed the opinion that the serious diagnosis and prognosis pronounced on the basis of the studies recorded above were neither justified nor rational, and that he would cure this young man in a very short time. However, we have definite information that he died after six weeks, following attempts at radiation therapy at another hospital.

From the illustrations accompanying this paper it can be seen readily that bone lesions of chloroma resemble early foci of multiple myeloma. The entire clinical picture, of course, is quite at variance.

Tumors of bone occurring in multiple members of the same family are not observed frequently. We record one such instance, as follows:

Case No. 84641. White female, aged 15 years, was hit on the lower part of the right thigh by a hard-pitched baseball, in September, 1931. One-quarter year later swelling occurred, with tenderness on use of the extremity and on pressure. Distress was particularly annoying at night. In May, 1932, when presenting herself at this institution, a tumor mass, hard to touch, and tender, about half the size of a large orange, was found over the inner right femoral condyle. On roentgenographic examination a malignant osteogenic tumor was observed, which we thought to represent a primary chondromyxosarcoma (Fig. 4-*A*).

In June, 1932, 18 x-ray treatments were given to the tumor area from two ports, to a total of 2,700 r, employing the Pfahler technic. No metastases were discovered anywhere. Subsequent roentgenologic examination (Figs. 4-*B* to 4-*G*) showed a continuous slow enlargement and expansion, culminating in an incomplete spontaneous fracture on Sept. 27, 1932. On October 10, amputation was performed well above the tumor by Dr. F. H. Purcell. The histologic report follows:

"Arising from the lower end of the femur is a newgrowth which is infiltrating the soft tissues. It is lobulated, grayish-white in color, and measures 10 × 8 × 8 centimeters in size. It is attached to the femur by a broad base. The bulk of the tumor is soft but spicules of bone are present."

Microscopic Findings.—"The tumor tissue is highly vascular and cellular and contains small spindle cells to medium sized giant cells. There is much variation in size and shape of nuclei, quantity of cytoplasm and in staining quality. Many small areas of calcification are present."

Diagnosis.—Osteogenic sarcoma of the femur.[2]

This patient is alive and well to-day without any evidence of metastases.

About three years after we had first seen this girl her father presented himself, complaining of a tumor in the region of the manubrium sterni, and of pain in the back and legs. A mass had been present in the sternal region for two months and was slowly enlarging. Simultaneously lumbosacral backache became more intense. Besides a severe oral sepsis there was found a firm mass about two and one-half inches in diameter, protruding from the lower part of the sternal manubrium. Furthermore, on clinical examination the upper mediastinal area seemed widened to the left. Roentgenologic examination of the chest (Fig. 5) showed a lemon-sized tumor arising from the left hilum. Structure of the thickened sternal manubrium appeared quite loosened up, honeycombed, and there was a flat retrosternal soft tissue tumor. A lumbosacral anomaly and some lumbar spondylitis, but no sign of tumor, was discovered in the spine.[3] Radia-

[2] We regret that histologic sections of this growth are no longer available for illustration.

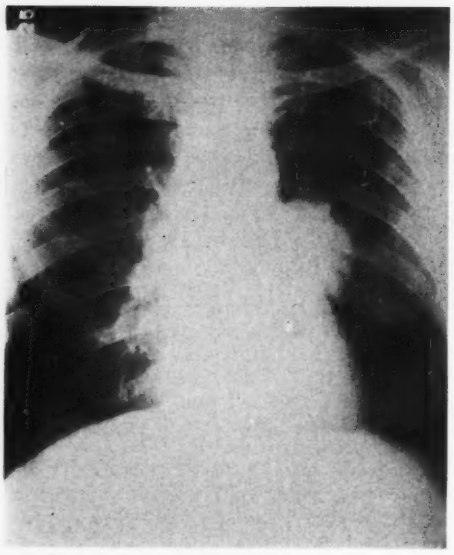


Fig. 5.

tion therapy was applied to the sternum and mediastinum from two ports for 23 days. A modified Coutard technic was used for a total of 5,340 r of heavily filtered radiation. During our observations no very material change occurred in the roentgen appearance of this patient's new-growth but arborization of the lung-fields became moderately intensified. This might have been the result of either radiation therapy or vascular stasis. During our observation this patient failed considerably and became quite irrational, so that he finally had to be transferred to the County Hospital. There a biopsy from the sternum was taken but proved unsatisfactory for histologic examination. A request for further study was refused by the patient, and he died six weeks after he had been seen by us for the first time. No autopsy was secured.

If we were inclined to accept case histories at their face value there would be no indication in either of these two patients' charts of the occurrence of an osseous neoplasm in multiple members of this family.

[3] Roentgen records of the sternum are not suitable for reproduction.

It is not our intention to draw untenable conclusions from the results of the therapeutic measures employed. The difficulties in evaluation of case histories, particularly in regard to tendencies of inheritance, however, we want to stress—speculation as to possibly aggravated malignant tendencies in subsequent generations is left to the reader. We regret sincerely that material for a final histologic diagnosis in this last patient could not be secured, and probable metastasis to the brain could not be proven, as primary tumors of the sternum are extremely rare and metastases to this patient's brain were suspected from his behavior.

Primary osteogenic tumors of the cranium are quite rare. We report herewith an osteochondrosarcoma which during the time of its observation became decidedly more malignant in character and ultimately led to the patient's death.

Case No. 88258. White female, aged 21 years. From the past history one might merely mention that she had been afflicted repeatedly with sore throats and peritonsillar abscesses. She had also suffered from pleurisy two years prior to admission. When entering our institution she complained of headaches, which had prevailed for about one year. This distress was first localized to the frontal region but lately had been quite generalized throughout the head and occurred in increasingly frequent attacks and with more intense severity. One month prior to admission an itching sensation was noted to the left of the bridge of the nose in which region within a week a rapidly growing tumor developed, extending to the supra-orbital ridge and the upper left lid, thus somewhat impairing vision of the left eye. During the development of the growth dizziness became quite annoying, as it was sufficiently severe to prevent maintenance of erect posture. On the advice of a physician the patient had all upper teeth and all lower molars removed four weeks prior to admission in order to alleviate her headaches, and also underwent at the same time a tonsillectomy. The extent of the tumor can be

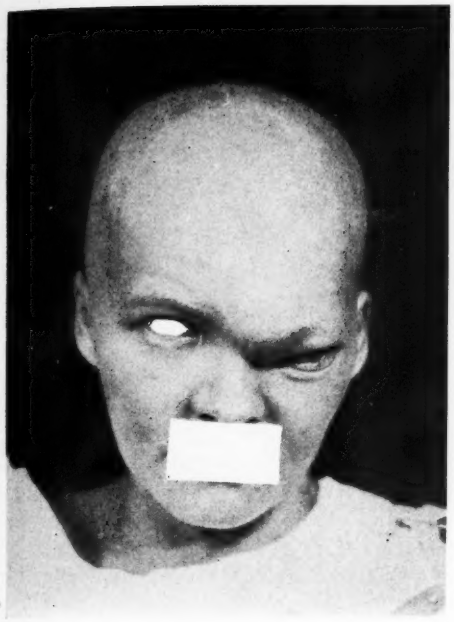


Fig. 6.

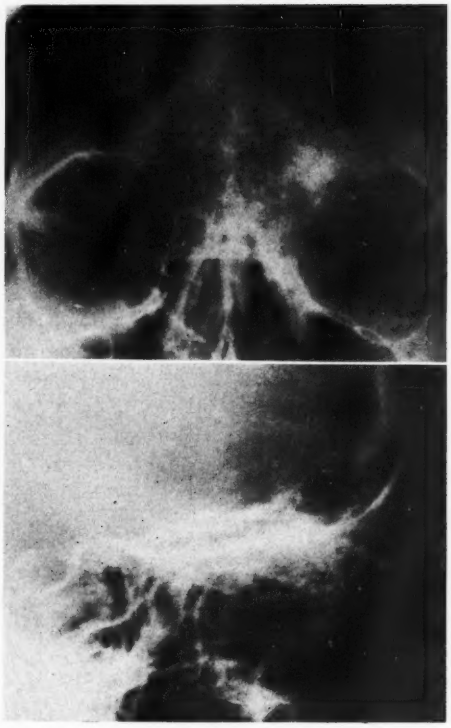


Fig. 7.

recognized in Figure 6, for which I am indebted to Dr. Edgar A. Kahn, of the Department of Neurosurgery at the University of Michigan.

Roentgenographic examination revealed an osteogenic tumor of highly granulated appearance, filling practically the entire frontal sinus, destroying a considerable portion of the left orbital roof and invading the cranial cavity by destruction of the inner table of the frontal bone dorsomedially to the orbital roof. It also extended into the left upper anterior ethmoidal area (Fig. 7). While we could not definitely identify this tumor, we suggested for differential diagnosis endothelioma and psammoma. Within a month's time it was apparent that in spite of radiation treatment—nearly 1,400 r were given to the tumor field from three ports or a total of 4,200 r during a period of three weeks—the neoplasm was enlarging in all directions.

Dr. Gurdjian removed some of the tumor tissue for histologic investigation, Dr. C. I. Owen reporting as follows:

"The specimen is composed of a small amount of well differentiated dense fibrous tissue and a parenchyma of a typical cartilage tissue. The cartilage tissue is highly cellular, somewhat undifferentiated, and the matrix is deeply stained. The exact degree of malignancy is not evident. These tumors recur on incomplete removal and become malignant at times. Diagnosis: Chondroma."

This patient was transferred to the Department of Neurosurgery at the University of Michigan and for information on her subsequent fate I am indebted to Dr. Edgar A. Kahn. He reported that Dr. Peet made an attempt to remove the huge tumor which projected out on the forehead and also invaded the various accessory sinuses. Grossly, he felt that he had succeeded, though it was an exceedingly radical operation. Dr. Weller's report was osteochondrosarcoma, not sufficiently cellular to give rise to metastases. A recurrence took place a few months later

and Dr. Peet made another attempt to remove the tumor. Dr. Weller's report was osteochondrosarcoma, becoming progressively more cellular. Dura and skin showed penetration at this time. He stated that the neoplasm had reached the stage at which metastases might occur at any time. Another operative attempt was made about eleven months after we had seen this patient first. Then, the tumor, according to Dr. Weller, had become even more cellular. A large portion of the scalp was necessarily removed and it was hoped to obtain a granulating surface which might later be grafted. The patient, however, died of meningitis a day or two later. No autopsy was obtained.

While from the original roentgenologic investigation we were not able to determine the type of tumor present, we felt from the beginning that it presented decidedly malignant characteristics. The lack of response to rather intense radiation therapy should be noted and also the tendency to increasingly malignant characteristics in the histologic structure in spite of this radiation treatment.

We know of but very few primary tumors involving the pubic bone and, therefore, record two nearly identical Ewing's tumors (endotheliomas).

Case No. 10098. White female, aged 14 years.[4] The past history was entirely irrelevant. For two months prior to admission this patient had noticed an ache in her right thigh which gradually became quite severe, so that she was unable to bear any weight on this leg. No history of injury. Examination revealed a slightly under-nourished, somewhat anemic looking young girl. There was tenderness over the right pubic ramus and the femoral ring, while otherwise she seemed to be quite healthy. Motion of the right hip was somewhat limited. Blood count showed 7,400 white blood cells. Temperature, 101 degrees, fluctuating later between 99 and 102 degrees. From the original roentgenologic examination Dr. Church reported as follows:

"The upper right pelvic ramus showed some mottled rarefaction with apparent expansion of the bone and periosteal lines along both inferior and superior surfaces. The acetabular cavity did not appear to be involved. Probably a low-grade bone infection or possibly a Ewing's sarcoma. The latter is a comparatively rare tumor and, therefore, it is much less likely than the former. We cannot, however, rule it out with absolute certainty."

On subsequent examination it was apparent that a somewhat laminated appearance became more noticeable along the pubic ramus, while concurrently destruction increased, leaving a somewhat striated texture (Figs. 8-*A* and 8-*B*). When we saw this patient I felt personally that an osteomyelitic process was more probable than an osseous neoplasm. At the suggestion of Dr. R. H. Stevens, radiation therapy was instituted. Two series of treatments were given in two subsequent months, the first consisting of two ports to the tumor region, each receiving 1,000 r of heavily filtered radiation, while in the second series about 950 r of heavily filtered radiation was applied to identical ports. The illustrations accompanying this article (Fig. 8) show the response of the growth to radiation or, rather, the lack of response to the doses administered. Subsequently Dr. R. G. Owen submitted the following histologic report on a biopsy:

"The entire mass of tissue consists of a newgrowth composed of rather small polyhedral cells with deep-staining nuclei. A moderate number of cells exhibit mitotic figures. The cells in some areas show an alveolar type of arrangement, while other areas exhibit a definite peritheliomatous structure. In still other places the cells lie in thin sheets, adherent to delicate connective tissue stroma. There is considerable necrosis of the newgrowth in certain areas and in these places lymphocytic infiltration has occurred. There is no evidence of differentiation toward cartilage or bone formation, nor are any giant-cell forms seen, Diagnosis: Malignant sarcoma of bone (Ewing's sarcoma type)." See Fig. 10-*F*.

[4] For much of the information concerning this patient I am indebted to Dr. Church and Dr. Poole, of Pontiac, Michigan, who had this patient under observation at the Pontiac General Hospital.

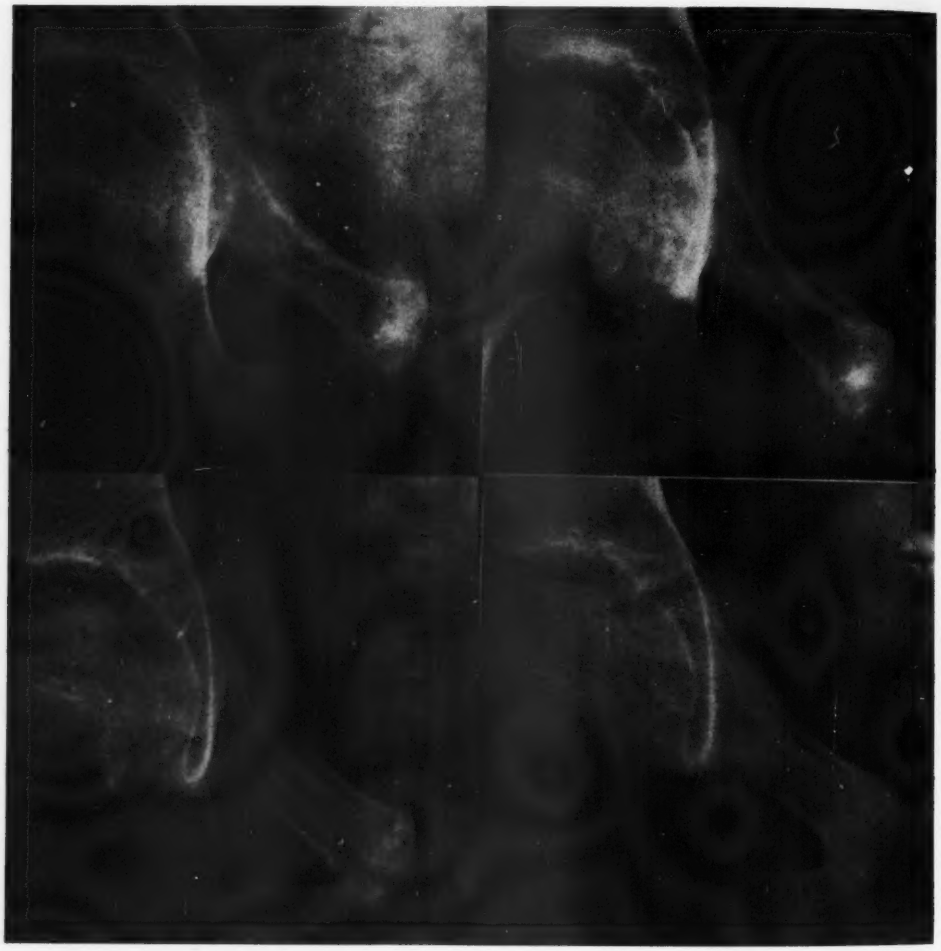
Six months after the first examination metastases were found in the right ilium and also multiple metastatic nodules were found in both lungs. The patient died soon thereafter.

The difficulty of differentiation between osteomyelitis and endothelioma of bone has been pointed out repeatedly in the literature. Usually it is stated that this type of tumor responds readily to radiation

Fig. 8.

therapy of moderate intensity. Such was not the case in this instance as is apparent from the illustrations.

A 6-19-34 B 8-7-34



C 12-8-34 D 1-5-35

Fig. 9.

About three years later an almost identical case came under our observation.

Case No. 9426. White male, 12 years of age, complaining of rheumatic pain in the right leg for the last month, during which period also a growth in the right groin appeared which had been receding somewhat in size of late. There was no history of injury. Physical examination was negative except for the presence of two masses in the right groin below Poupart's ligament and under the sartorius muscle. Tuberculin tests were negative; tests for syphilis were negative. Blood count showed 3,400,000 red blood cells, 10,000 white blood cells, 70 per cent polymorphonuclears, 28 per cent mononuclears. Urinalysis was negative. Temperature was almost normal. The roentgenologic diagnosis of a Ewing's tumor was made from the first examination (Fig. 9-*A*). Sub-

sequently exploration and curettage were performed (Dr. D. M. Stiefel). He found a shiny, dome-shaped tumor of distinctly dark olive-green color. On incision there discharged under considerable pressure a material resembling pus mixed with blood and nondescript detritus.

Histologic Examination (Fig. 10-*G*).—Dr. C. I. Owen furnished the following:

"The soft tissues are widely infiltrated with tumor tissue. This tumor tissue is composed of cells which in general are small, varying from small circular densely staining cells to small spindle cells with elongated nuclei. The bulk of them are the latter. It is a highly vascular tissue and includes much hemorrhage. There is a slight capillary architecture. Diagnosis: Ewing's tumor of the bone."

Two series of x-ray treatments were given. At first, 1,800 r of heavily filtered high voltage radiation was applied to each of two ports in twenty days. At the second series, a little over two months later, 1,500 r of heavily filtered high voltage radiation was applied to two ports each. At this time the patient was quite comfortable and was up and around. The response of the neoplasm to this radiation treatment is well shown in Figures 9-*A*–9-*D*, remarkable repair resulting in the invaded bone to an ultimate architecture almost resembling healing of the lesion.

In April, 1935, this boy returned to the hospital with pain in shoulders and chest. An increasing opacity of the right chest was observed, interpreted as a spreading bronchopneumonia with considerable congestion in the left lung. Roentgen examination of skull, shoulders, and mandible revealed no demonstrable evidence of invasion by neoplastic metastases. However, the boy succumbed to his disease on May 28, 1935. No autopsy was obtained; therefore we could not ascertain presence or absence of pulmonary or other scattered metastases.

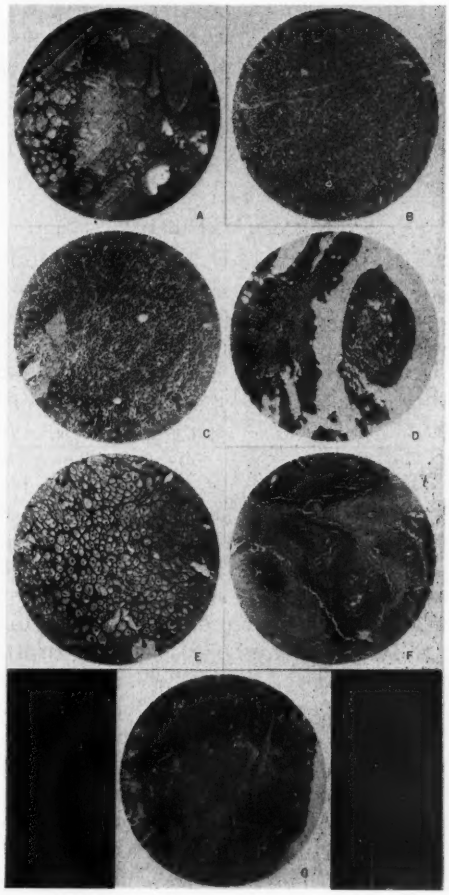


Fig. 10.

SUMMARY

Ten cases of neoplasm involving the skeleton are reported: One metastasizing adenoma of the thyroid; three multiple myelomas; one chloroma; one osteogenic sarcoma of the femur; one tumor of the sternum—not classified; one chondrosarcoma of the frontal bone; two endotheliomas of the pubic bone.

The noteworthy features of these cases are pointed out. Only one of these patients is surviving and apparently cured definitely.

TEMPORAL BONE STUDIES

By E. M. SHEBESTA, M.D., *Detroit, Michigan*

From the Radiologic Services of R. H. Stevens, M.D.; H. A. Jarre, M.D., and C. K. Hasley, M.D., Grace Hospital

TECHNICAL CONSIDERATIONS

IT IS our impression that there are still too few roentgenologists who routinely examine the mastoid region in more than one plane: it is this fact which prompts the writing of this paper. No other bone in the body is studied in only one plane, and a bone as anatomically complex as the temporal bone should be no exception.

The following men have described positions to be used in the examination of the temporal bone: Law, Schüller, Stenvers, Taylor, Chamberlain, Henle, Lange, Sonnenkalb, Feretti, Fisher-Sgalitzer, Busch, Mayer, Groshey, Staunig, Graupner, Kuhne and Plagemen, Lysholm, Löw-Beer, Hasselwander, Hirsh, and others. At least 24 different projections have been described. When the roentgenologist is confronted with this multitude of projections he naturally is bewildered. Most of us are agreed on the Law-Schüller projection as a necessity: the confusion arises when the other planes are to be employed. Several of the advocated projections are useful in demonstrating some particular involvement of the temporal bone such as acoustic nerve tumor, disease of the mastoid tip, etc. Some of the objections to the different methods are complex technic, distortion, and discomfort to the patient.

Roentgenologists need not concern themselves with the multitude of methods for rarely does one need roentgenograms made in more than two planes for the same reason that we use only these two planes in studying other bones. We, therefore, routinely employ the usual Law-Schüller projection and the Stenvers' projection. These two methods enable one to view the temporal bone in the postero-anterior and lateral planes and only very rarely do we use the mento-vertex or vertex-mental projection. In the examination of the pars petrosa, the Stenvers' view (see Fig. 1) is the most widely used in Europe and is gaining popularity in this country very rapidly. The Stenvers' view demonstrates all the essential anatomy of the pars petrosa as well as the minute structures of the middle ear with the least amount of distortion. Our technicians have had no difficulty with this method. If one wishes to simplify the technic he can use the device recommended by Sussman (19), or the Camp and Gianturco localizer. It is well to remember that the mastoid tip and the lateral portion of the mastoid are less radio-opaque than the pars petrosa, and consequently when we are particularly interested in this region we reduce the exposure approximately 25 per cent. By using stronger illumination this additional exposure is usually not necessary. We have not found the Potter-Bucky diaphragm essential. Likewise, no special means of immobilizing the head are required if a short exposure can be used. A fine focus tube and a small cone are highly desirable.

ROENTGEN INTERPRETATION

The roentgenologist should be prepared to answer the following questions: Is the mastoid process cellular or non-cellular; is there evidence of cell destruction; is there evidence of softening of the bone; if a previous operation has been performed, how much of the cell structure remains; what is the position of the mastoid foramen; is there any evidence of tumor involving the temporal bone; what relation does the lateral sinus bear to the affected region; what is the extent of pneumatization of the petrous bone; does the infectious process involve the petrous bone, and if so, is there evidence of suppuration and

bone destruction? These questions can be answered more accurately by studying the temporal bone in more than one plane.

a syndrome which is now known by his name. The syndrome, associated with suppuration of the pars petrosa, consists of

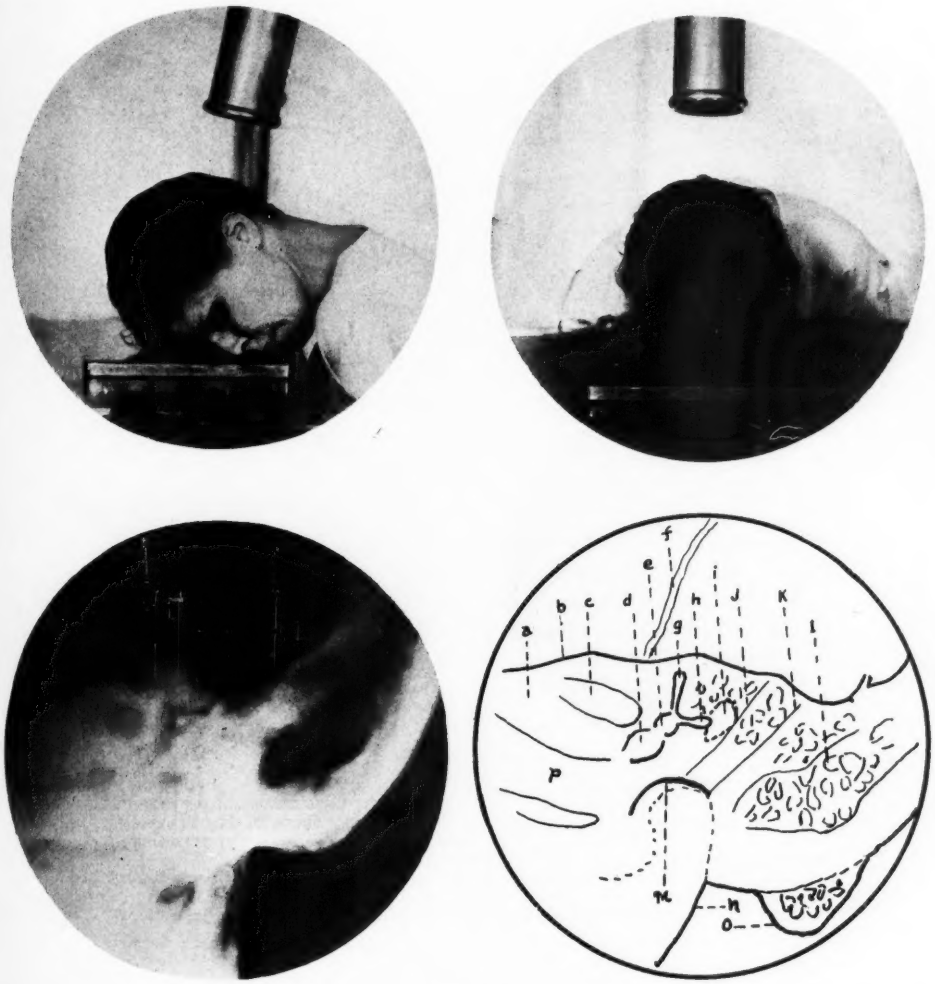


Fig. 1.

(*Upper left*) Stenvers' position. The head rests on the orbit, nose, and maxilla. The roentgen tube is tilted 12 degrees cephalad.

(*Upper right*) Stenvers' position. The sagittal plane of head is at a 45 degree angle to the cassette. The rays traverse the pars petrosa perpendicularly.

(*Lower left*) Stenvers' view of a normal bone.

(*Lower right*) Diagram of the roentgenogram (*lower left*). *a*, Petrous apex; *b*, roof of petrous pyramid; *c*, internal acoustic canal; *d*, cochlea; *e*, vestibule; *f*, middle meningeal artery marking; *g*, superior semicircular canal; *h*, horizontal semicircular canal; *i*, region of antrum; *j* and *k*, wall of lateral sinus; *l*, mastoid cells; *m*, temporo-mandibular joint; *n*, mandibular condyle; *o*, mastoid process; *p*, zygoma.

The greatest value in multiplane examination of the temporal bone is in the diagnosis of suppuration in the pars petrosa. As early as 1904, Gradenigo (7) described sixth nerve paralysis, fifth nerve pain, and a discharging ear. However, it was not until after the excellent papers of Kopetzky, Almour, Eagleton, Profant, and Tay-

lor, in 1930 and 1931, that suppuration of the pars petrosa was diagnosed prior to autopsy except in rare instances. Profant

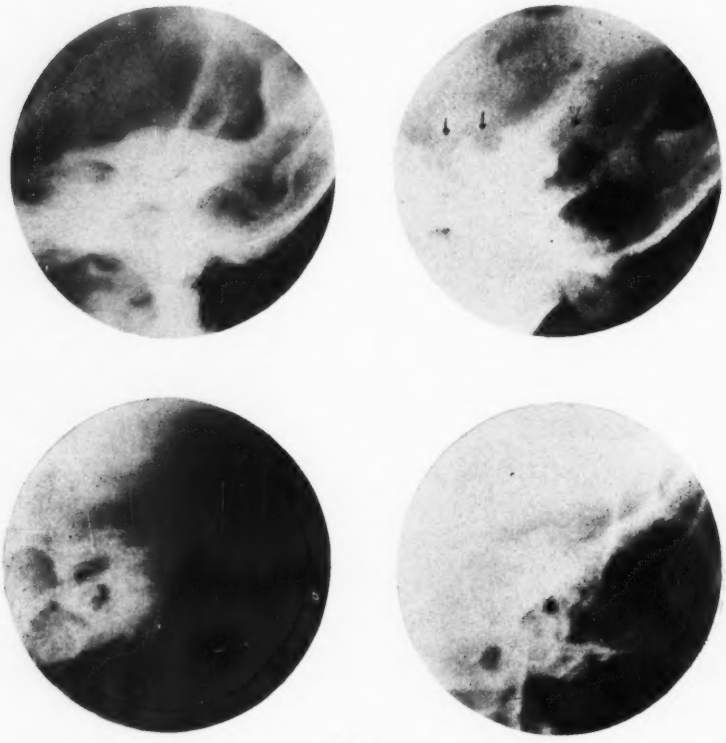


Fig. 2.

(*Upper left*) Normal side.

(*Upper right*) Pathological side. Notice the marked destruction of the petrous ridge and petrous apex. The clinical and roentgenologic diagnosis was petrositis. Six weeks prior to these studies a mastoidectomy was performed, with positive findings of mastoiditis. At autopsy a meningioma was discovered

(*Lower left*) Law-Schüller projection showing destructive mastoiditis, but the perforation is not demonstrated.

(*Lower right*) Stenvers' projection showing the mastoiditis as well as the perforation.

(17), in 1930, read at the American Medical Association meeting a paper on Gradenigo's syndrome, at which time he suggested the use of the term "petrositis." He had dissected the temporal bones of five-, six-, and seven-month fetuses, two full-term infants, and 100 adults, finding three types of bone formation: (1) compact or sclerotic, (2) spongy or cancellous, and (3) cellular. Profant also studied the routes of infection in cases of petrositis and concluded that there are two routes:

"(1) *The 'antrum epitympanic route.'*—The cells extend from the antrum and epitympanic spaces above the cochlea, and above and behind the superior semicircular canals; then behind, above, and in front of the internal auditory meatus, and finally to the mass of cells under the tegmen of the anterior surface of the tip.

"(2) *The 'hypotympanic route.'*—The cells extend from the hypotympanic space below the cochlea, then below the internal auditory meatus, and finally to the mass of cells under the tegmen of the posterior surface of the tip."

Heretofore the four routes described by Perkins have been generally accepted.

It is well to remember that the type of

bone formation found in the pars petrosa does not necessarily parallel that of the mastoid portion. Belinoff and Balan (1) found the two portions the same in 37.5 per cent of 40 temporal bones studied. The types of bone formation found by them were 35 per cent pneumatic, 22.5 per cent diploic, and 42.5 per cent contained mixed cells. Other authors have found relatively similar findings, but Profant believes the cell formation is similar in the two portions of the temporal bone.

Petrositis may occur irrespective of the cell formation. When the pars petrosa is not pneumatized the process is an osteomyelitis. However, petrositis is most commonly found in pneumatized bone. Routine examination of the pars petrosa is urged in order to recognize an early case of petrositis as well as to furnish a control roentgenogram if later complications arise. The roentgen findings of petrositis are similar to those of mastoiditis, namely, cloudiness followed by evidence of cell erosion and later evidence of abscess formation, sclerotic changes, or—in advanced cases—complete disappearance of the contour of the petrous apex. Usually some clouding is noted in the pars petrosa accompanying a simple mastoiditis. Kopet-

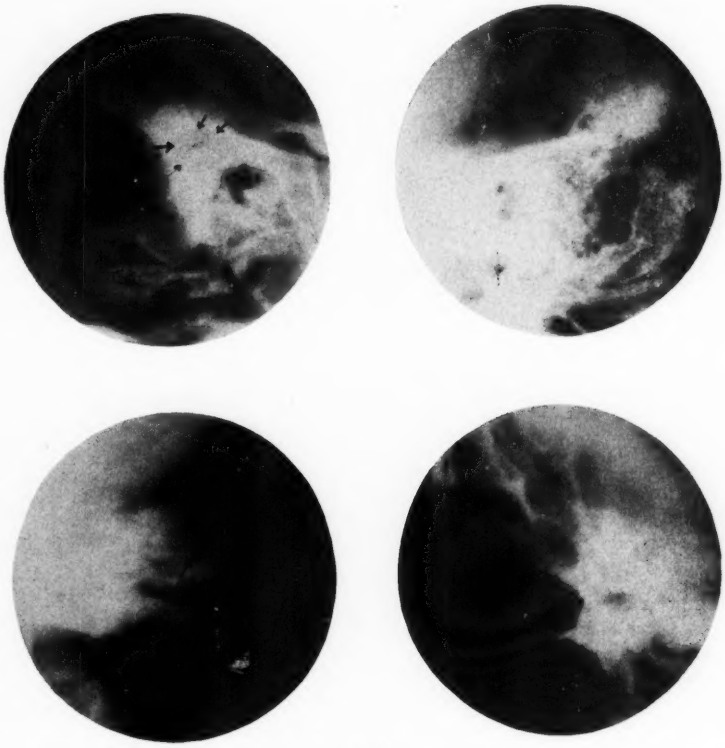


Fig. 3.
(*Upper left*) Notice the large defect which was produced by a cholesteatoma (Law-Schüller projection).
(*Upper right*) The opposite mastoid. Notice the difference in pneumatization between the two mastoids of the same patient.
(*Lower left*) Same region as in previous view (Stenvers' projection). Notice the cholesteatoma. The depth at which the surgeon shall find it is clearly demonstrated. Notice the slight degree of pneumatization.
(*Lower right*) The opposite mastoid. A lighter exposure is required to demonstrate the mastoid process.

zky, Almour, and Taylor have found the injection of lipiodol helpful in studying the diseased pars petrosa. The lipiodol is instilled through the fistulous tract or through a drill hole made by the Almour operation. This appears to be the only way to demonstrate perforation of the petrous apex.

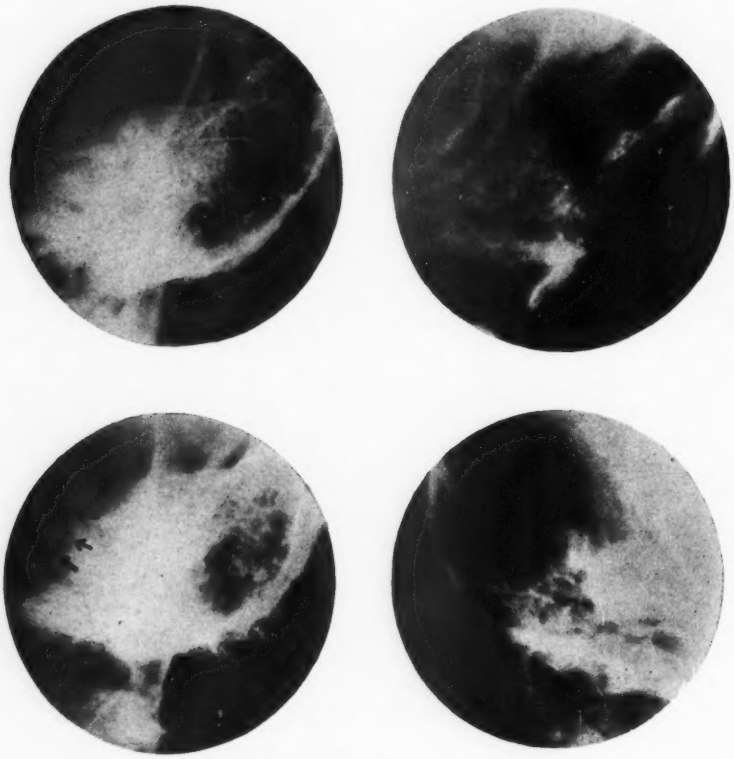


Fig. 4.
(*Upper left*) Early destructive mastoiditis (Stenvers' projection).
(*Upper right*) Same region 30 days post-operatively. Notice the post-operative defect as well as destruction in the petrous pyramid.
(*Lower left*) Another case. Notice the defect in the petrous apex as well as destructive mastoiditis (Stenvers' projection).
(*Lower right*) Stenvers' view of another case. Notice the numerous "punched out" defects in the temporal bone which were proven to be chloromatous foci. Other parts of the skeleton were also involved. (See Dr. H. A. Jarre's article in this issue.)

The clinical findings of petrositis will be discussed briefly. Gradenigo's syndrome is not a common finding in petrositis. In a series of 15 cases observed by Kopetzky and Almour, only two cases showed sixth nerve paralysis. Abductor nerve paralysis is due to disease of a pneumatized pars petrosa in the region of Dorello's canal through which the nerve passes. Ocular or facial paralysis and pain along the distribution of these nerves is a much more important sign. The eighth nerve is also frequently involved. All these nerves are in close proximity to the pars petrosa and are affected by the neighboring swelling and congestion. The most frequent findings are low grade sepsis, otorrhea, retro-orbital pain, and occasionally sixth nerve paralysis. These findings usually occur several weeks following a mastoidectomy.

Those who are interested in the treatment of petrositis are referred to the ar-

ticles of Eagleton, Kopetzky and Almour. However, very close co-operation between the otologist and roentgenologist is necessary since early operative treatment occasionally will prevent a fatal meningitis, and occasionally an unnecessary operation may be avoided since many cases of petrositis clear up spontaneously.

Other conditions which may be demonstrated by multiplane examinations are periostitis of the mastoid process with pus between the bone and periosteum; swelling of the external ear resulting from furunculosis of the external auditory canal; Bezold mastoid with perforation of the tip; necrosed bone covered by normal cell structure, and acoustic nerve and cerebello-pontine angle tumors. Acoustic nerve tumor produces an enlarged internal auditory meatus with surrounding rarefaction. In one of our cases (Fig. 2) we incorrectly diagnosed petrositis, and at autopsy a meningioma was found producing the osteonecrosis of the pars petrosa. This case, however, previously had had mastoiditis, and at the time of the roentgen examination she had diplopia, pain in the ear, and purulent discharge from the ear, all of which are typical symptoms of petrositis. Petrous ridge deformities may also result from cerebello-pontine angle tumors, as pointed out by Pancoast (15).

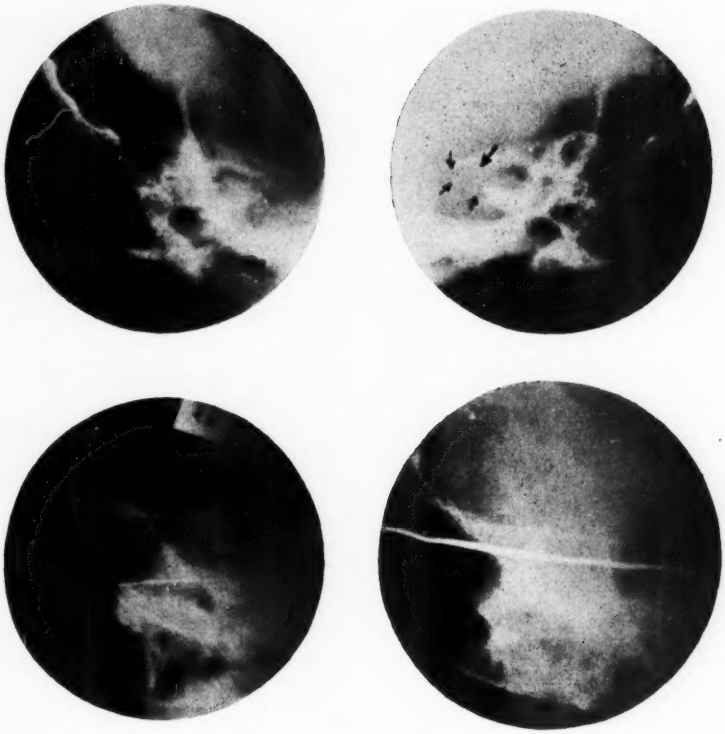


Fig. 5.

(*Upper left*) Stenvers' projection showing otitis media and early destructive mastoiditis.

(*Upper right*) Same case but the opposite side, showing also a mastoiditis as well as an early petrositis. (Cerebro-spinal fluid showed increased cell count and later also streptococci.)

(*Lower left*) A case of sclerosing petrositis.

(*Lower right*) Another case showing marked destruction in the petrous apex. Notice the probe in the apex.

SUMMARY

1. Temporal bone examination is in a state of confusion and a more uniform practical method is highly desirable.

2. Routine examination of the temporal bone in more than one plane is strongly urged.

3. Several illustrative roentgenograms are presented.

I wish to express my appreciation to Dr. Hans A. Jarre for his valuable assistance.

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CONGENITAL BONE DYSPLASIA

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THERE is probably no tissue in which the histological picture is more complicated than that of the osseous system. During the life of the individual there is a constant metaplasia, each phase of which may proceed at different rates during different periods.

This makes possible an infinite number of pathologic changes, depending on the phase of bone growth affected, the period at which this takes place, and the degree and type of histopathologic change. Similar etiological factors may cause widely different conditions as seen clinically, microscopically, or radiographically.

It is not difficult to understand, therefore, that in reviewing any group of pathologic bone conditions one is confronted with a complexity of nomenclature and classification. This is especially so in dealing with the bone dysplasias as little, if anything, is definitely known concerning the etiology of those conditions. There is no general agreement except that the conditions are not tuberculous, rachitic, or syphilitic, but rather congenital, with some types showing definite hereditary tendencies.

The congenital bone dysplasias can be roughly divided into two main groups, (1) the malacic, in which the predominant characteristic is a deficiency in sub-periosteal bone production with a resultant softening and osteoporosis, and (2) the hyperostotic, in which there is over-production of cortical bone.

Osteogenesis imperfecta.—This condition is classified as a myeloplastic malacia by Hirsch (6) in his modification of von Recklinghausen's classification of the malacias. Two forms of osteogenesis imperfecta are generally recognized, depending on the age at which the condition appears.

Osteogenesis imperfecta congenita.—First described by Vrolik, in 1849, numerous cases have been reported of this interesting condition. It is characterized by multiple fractures which show evidence of healing *in utero*. The long bones, ribs, and clavicles are most often affected. The very thin cranial and pelvic bones are poorly developed and all the bones show osteoporosis to a more or less marked degree.

The disease is incompatible with life, most patients surviving only a few hours. Some have been reported as living as long as two or three weeks. The infants are always born to normal parents and the most plausible cause for the disease appears to be a primary defect of the mesenchyme, as held by Weber (13). An interesting case has been reported by Welz and Lieberman (14), as occurring in single ovum twins.

These authors and others have investigated the blood chemistry in the patient and parents and find no variation from the normal. Wyatt and McEachern (16) have reported unusual vascularity of the parathyroids in one case. An endocrine etiology is generally considered, however, to be purely an assumption, as this is the only instance in which any of the endocrine glands have been discovered to be abnormal.

The author's case (Fig. 1) demonstrates the typical multiple fractures, most of which show evidence of healing *in utero*. Also to be noted is the thickening and shortening of the long bones, described by Fairbank (2) as Type I. The cranial bones are extremely thin, although the pelvic bones do not show this characteristic to any great extent.

The history in this case is also typical of that usually reported. The mother was a primipara, 20 years of age, apparently in excellent health, and the puerperium was uneventful and of normal duration. Delivery was by breach, as is almost invariably the case, and the infant expired in less than one hour. The maternal and

cord Wassermann reactions were both negative. No family history of bone disorders could be elicited on either side.

The fractures are usually incident to some minor trauma and occur almost always in the diaphyses of the long bones or

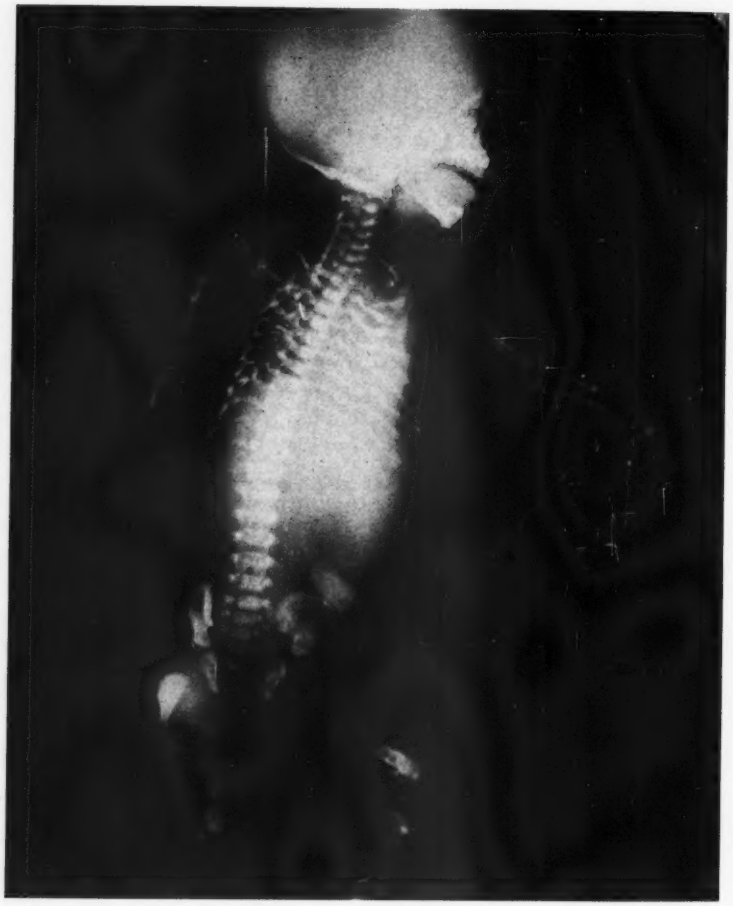

Fig. 1.

Osteogenesis imperfecta tarda.—Terms frequently used synonymously are *osteopsathyrosis* and *fragillitas ossium*. I believe the term *osteogenesis imperfecta tarda* is preferable since there appears to be very little difference between this condition and *osteogenesis imperfecta congenita* except that the manifestations are less severe and not present at birth. It was first described by Lobstein in 1833 and often is referred to as *Lobstein's disease*.

in the ribs. Cases have also been reported involving the fingers, mandible, patella, and pelvis. The femur is by far the most common site. Goin (3) reports that the average age at which the first fracture occurs is between the second and fourth year. The great majority occur between the ages of three and eleven, and they are uncommon after the age of twenty. The total number of fractures varies considerably although it is unusual to witness more than

ten. Healing takes place rapidly, and there is often considerable deformity, due to malunion.

The roentgen findings are similar to those seen in osteogenesis imperfecta congenita. There is a high degree of osteoporosis and the cortex is very thin and deficient in lime salts. The long bones, however, tend to be long and narrow—Fairbank Type II— and show deformities from malunion of previous fractures.

There appear to be two types of osteogenesis imperfecta tarda: (1) The idiopathic, or non-hereditary, and (2) the hereditary type in which the condition is part of a syndrome in which the presence of blue sclera is a dominant characteristic.

The latter condition was first described by Spurway (12), in 1896, and has since been frequently discussed, usually under the head of "brittle bones and blue sclera." Because of its hereditary nature and the fact that structures derived from the mesenchyme are primarily affected, Key (9) prefers the term "hereditary hypoplasia of the mesenchyme."

If the disease is due to a primary defect in the mesenchyme, the question arises as to why all the tissues derived from this structure are not affected. Shugrue (11) states that probably all these tissues are involved to a varying degree with the more highly organized group comprising the bones, cartilage, and tooth pulp showing the greatest disturbances.

Blue sclera is a dominant characteristic and is always present, both in the patient himself and in one of his parents. There is no skipping of generations. Associated with this, one may or may not have any or all of the following:

(1) Multiple fractures—70 per cent cases.

(2) Deafness. This is of the otosclerotic type and does not appear until later in life, usually about the twentieth year. For this reason, it has probably not been reported as often as it actually occurs.

(3) Loose joints and frequent dislocations and sprains due to laxness of the fibrous structures of the body.

The treatment of cases of osteogenesis imperfecta tarda, either of the hereditary or idiopathic type, is, of course, symptomatic with special attention given to proper alignment of fractured bones and precautionary measures to avoid new fractures. Hansen (4) reports a thorough study of the mineral metabolism in two patients to whom large doses of viosterol and parathyroid extract were administered. He concludes that "while it cannot be concluded that hyperfunction of the parathyroid is a factor in osteogenesis imperfecta, it is obvious that large doses of viosterol or parathyroid extract only accentuate the condition already present in mineral metabolism and are contra-indicated as therapeutic agents in this condition."

Osteitis fibrosa and osteitis deformans.—Although the *osteitis fibrosa* of von Recklinghausen and the *osteitis deformans* of Paget are generally recognized as two distinct disease entities, nevertheless the pathological processes are fundamentally similar. These consist of fibro-osteoid change, malacia, giant-cell tumor formation, and hyperostosis.

Osteitis fibrosa is generally conceded to be a congenital bone dysplasia with relatively strong hereditary tendencies. In his comprehensive work covering this condition, Hirsch (5, 6, 7) states that here also a congenital weakness of the mesenchymal tissues may well be the underlying cause. Lesions of the parathyroids have been suggested as a possible etiological factor, but as yet there is little to substantiate this assumption.

Osteitis deformans is regarded as an affliction of later life. This is probably due, in part, to the fact that the condition is not usually recognized until deformities present themselves. The progress is slow, the symptoms are few, and the patient does not become concerned until noticeable deformities have developed. There appears to be an hereditary tendency and, if so, the changes have possibly been slowly progressing even since birth. The lesions may possibly have been present in childhood in the form of a mild and hence unrecognized form of osteitis fibrosa.

Osteochondritis.—Although this condition in its various manifestations is not generally regarded as congenital, there is no agreement as to the etiology and this assumption is permissible. Infection, endocrine disturbance, and trauma have been considered as basic factors, but there is little conclusive evidence to support these theories. Christie (1) notes that the locations in which the condition occurs are those which are subject to the slight but long-continued trauma of muscular pull, weight-bearing, and pressure, and states that this may interfere with the blood supply to the epiphysis during the period of rapid growth.

The most common site of involvement is the epiphysis of the head of the femur. This is the well-known *osteochondritis deformans juvenilis coxæ* described by Calvé and Legg and Perthes in 1910. The epiphysis of the tibial tubercle is also rather commonly involved under the term *Osgood-Schlatter's disease.* Less frequently affected epiphyses are those of the tarsal scaphoid and the head of the second metatarsal, both of which conditions are usually referred to as *Köhler's disease.* The latter also may be called *Freiberg's disease* or *Freiberg's infarction.*

Osteochondritis deformans juvenilis dorsi is an uncommon manifestation involving the vertebral epiphyses described by Scheuermann in 1921 and often called *Scheuermann's disease.* Various other epiphyses may become involved, such as those of the semilunar, os calcis and olecranon and the term *osteochondritis dissecans* is sometimes used in describing these conditions.

Congenital bone dysplasias which are characterized by hyperostotic changes comprise a small group of rare conditions. Hereditary and familial factors appear to be definitely present in the majority of cases reported.

Marble Bones.—This uncommon disease was first described in 1904 by Albers-Schönberg with whose name it is usually associated. Other terms are *congenital osteosclerosis* and *osteopetrosis.* The changes consist in an increase of hard cortical bone with partial or complete obliteration of the marrow cavity. The epiphyseal lines are still present but are irregular and the bones become hard and brittle, with resultant pathologic fractures. The condition is more or less generalized and occurs during the first age period. Karshner (8) believes a primary dyscrasia of the mesenchyme is responsible and the disease may begin *in utero.*

Melorheostosis.—A localized form of hyperostosis was first described by Léri and Joanny, in 1922, under the name of *melorheostosis.* The changes are confined to the bones of a single extremity and the involvement of the bones themselves is not generalized as in cases of marble bones. Léri described the radiographic appearance as that of wax along a candle and the term *flowing hyperostosis* is commonly used. In addition to the proliferation of cortical bone along the shafts of the long bones, irregular bony masses are deposited in the shoulder or hip which, as the condition progresses, may cause limitation of motion or fixation. Pathologic fractures have never been observed. The average age at which the first symptoms occur is 20 years. Kraft (10) states this may vary from five to 42 years, the progress being slow and the changes often remaining stationary for long periods.

Osteopoikilosis.—This condition probably cannot be rightly classified as a hyperostotic involvement. The areas of increased density seen in the roentgenogram have been shown to be condensation of bone rather than proliferation, hence the term *disseminated condensing osteopathy.* The first case was described by Albers-Schönberg in 1915. Wilcox (15) found 17 reported cases through 1932 and added two more which occurred in father and son. His cases are the only ones showing blood relationship.

The roentgen changes consist of small areas of increased density in the spongiosa of the epiphyses and metaphyses and have been demonstrated in all the bones except those of the skull. The condition is symp-

tomless and is only discovered during the course of roentgenographic examination for other causes.

SUMMARY

At present we must be satisfied by assuming that factors of unknown etiology disturb the delicate balance between bone absorption and new bone formation to produce the various bone dysplasias. Regardless of the etiology, it is evident that these factors may be present in early intrauterine life and in some instances, at least, are definitely hereditary. The prevailing pathologic changes are those of increased bone absorption and faulty bone regeneration, whereas the osteopathies which are characterized by excess production of cortical bone comprise only a small group of extremely rare conditions. The following classification is suggested:

Malacic

1. Osteogenesis imperfecta congenita.
2. Osteogenesis imperfecta tarda.
   (*a*) Non-hereditary or idiopathic.
   (*b*) Hereditary, associated with blue sclera.
3. Osteitis fibrosa cystica.
4. Osteitis deformans.
5. Possibly osteochondritis.

Hyperostotic

1. Marble bones.
2. Melorheostosis Léri.
3. Osteopoikilosis

The influence of the endocrine glands, especially the parathyroids and pituitary, upon bone growth is well recognized, but there is nothing to substantiate the belief that the congenital bone dysplasias are manifestations of endocrine dysfunction. Careful studies of mineral metabolism have failed to elicit any conclusive results.

A case of osteogenesis imperfecta congenita is reported, the various bone dysplasias of congenital nature are discussed, and an attempt is made at classification of these conditions.

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THE RELATION OF ROENTGEN THERAPY TO THE TREATMENT OF FIBROSARCOMA

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IT is generally stated in medical literature that fibrosarcoma is markedly radioresistant, and therefore recurrence or metastasis would indicate a hopeless prognosis. Consequently, it has seemed wise to study the cases of fibrosarcoma which have been referred to us for radiotherapy, either because of recurrence after operation or as a prophylactic measure following operative removal of the tumor. We have selected all of the cases of fibrosarcoma which have had radiotherapy, and have not included the cases which had surgery only.

The cases under consideration comprise only those of connective tissue origin. The benign fibromas and the more anaplastic types of sarcoma have been eliminated.

These tumors are commonly found in the skin and subcutaneous tissues, but in our series the point of origin was more commonly situated in the muscle sheaths or septa. Sex is not a differential point in the diagnosis as the distribution is fairly even. Such tumors may be found at any age, but in large reported series the preponderance of cases will be found in groups from the third to the seventh decades of life. They are somewhat more common in the third and fourth decades than is carcinoma. Antecedent trauma is not prominent in the history of these cases. French (1) reports that in only one case in his series of 16 cases was the cause of the tumor attributed to trauma. Stout (6) states that fibrosarcomas are sometimes found in cicatrices and that he has observed it personally in four cases. He also quotes from the literature cases in which these tumors have developed in areas subjected to prolonged irradiation. He believes, however, that these are of exceptionally rare occurrence.

The microscopic picture of these tumors is essentially fibromatous in character but has certain changes which characterize them as being malignant in nature. They are composed of interlacing strands of spindle cells and collagen fibers in varying amounts. There may be considerable variation in the size of the cells, and giant cells with multiple nuclei may be present. In general the malignant nature is shown by evidence of invasion, active mitosis, and anaplasia. Warren and Sommer (7) believe that "the most useful histologic criterion in determining a high degree of malignancy has been the presence of a fair to a marked number of giant cells." Mitotic figures are usually present in varying numbers, and if quite numerous usually indicate a malignancy of considerable activity.

French (1) states that when the nuclear material increases in proportion to the cytoplasm of the cells there is an increase in the mitosis and malignancy. He classifies these tumors in three groups according to the degree of malignancy: (1) Tumors of first degree malignancy were composed of spindle cells with a predominance of dense fibrous material and few cells. (2) In those of second degree malignancy there was less of the intercellular fibrosis. Large spindle cells in compact bundles were more prominent. (3) Tumors classified as third degree malignancy had little stroma, were highly cellular, and were made up of embryonic fibroblasts. In his cases the prognosis followed closely the histologic picture. The highly malignant forms recurred rapidly and the survival of the patient was short.

The symptoms produced by these tumors are usually slight. In most instances the patient is aware of a tumor mass for some months before increase in size and

the occurrence of pain brings him to a physician. In four, or 33 per cent of our cases, pain was part of the symptomatology. In one case a severe neuritis due to spinal metastases was the prominent feature of the case from the time of the first observation. Deep-seated tumors which invade other structures or exert pressure effects on neighboring organs may produce rather extensive symptoms from these effects. The anemia and loss of weight, which are usual with carcinoma, are absent in this disease.

Physical examination usually discloses a hard nodular circumscribed tumor of variable size. It is frequently fixed to the underlying structures and when removed may be larger than anticipated. In six of our cases the point of origin was in structures of the anterior abdominal wall; in five it was primary in the extremities, and in one, it was attached to the latissimus dorsi muscle.

Roentgen examination will frequently give useful information regarding these tumors, especially those situated in the extremities. The tumor may be seen as a circumscribed shadow of somewhat greater density than the surrounding soft tissues. It has the additional advantage of determining if there is any bone destruction or thinning of the cortex due to pressure atrophy. Periosteal thickening and irregularity of contour would suggest that the tumor was attached to the bone. In four of our cases these tumors could be visualized on the roentgen film. In one case local bone involvement was seen, and this was used as a guide in the future treatment of the case. In a second case bone changes secondary to radiotherapy could be differentiated from destruction of bone as seen in tumor destruction. In other cases bone destruction could be ruled out previous to operative procedures.

THERAPY

The problem of therapy in these cases is always a perplexing one due to the known tendency to local recurrence. In many instances a local excision is done under the impression that the tumor is benign, and recurrence is consequently prompt. One is faced then with the question of wide excision—or amputation, if the origin is in one of the extremities. An alternative method of treatment to be considered is radiotherapy.

Meyerding, Broders, and Hargrave (2), in reporting the results of treatment in a series of these cases at the Mayo Clinic, state that the results of amputation in 34 cases, in which there were no demonstrable signs of metastasis, showed only 14.7 per cent five-year cures. Many of their cases had had previous operations. In a series of 21 patients, who had had only one previous excision, there were 14.3 per cent five-year cures. These writers believe that early amputation would probably cure a much larger percentage of the cases but would mean unnecessary sacrifice of the limbs in some cases. They state that among all of their cured cases there was a predominance of sarcomas of low grade malignancy. Among 28 cured cases, four had excision only; one had excision and Coley's toxins; 17 had excision and radiotherapy; and six had amputation.

Quick and Cutler (3), in a comprehensive study of 75 cases of various types, report 10 amputations in tumors of the extremities. Five patients were well, and five died of pulmonary metastasis soon after amputation. In 15 cases of tumor of the extremities treated by local excision and radiation therapy, eight patients died and seven were well for from two to nine years. These writers believe that the method of choice in the treatment of operable tumors, with the exception of the very malignant type, is pre-operative radiation therapy followed by wide surgical excision and immediate post-operative radiation therapy before the remaining tumor cells become incarcerated in the dense post-operative scar. It is generally accepted that the tumor bed is an important factor in prognosis, in cases submitted to radiation therapy, and that tumor cells embedded in fibrotic scar tissue do not respond in the same degree as they

do when the capillaries and fibroblasts are abundant.

Warren and Sommer (7) reported a study of 163 cases of fibrosarcoma of the soft parts. Most of their cases were treated surgically. They found recurrence in 64 cases, and of these only eight patients were alive three years after treatment of their last recurrence. They state that recurrence is rare after the first year. A few of their cases received post-operative radiotherapy without any beneficial result, and several recurrent cases progressed in spite of active radiation therapy. They report five cases in which the tumor was associated with irritative stimuli of various kinds, and in two of these cases the growth developed in scars resulting from radiation therapy administered many years before.

French (1) studied a series of 16 cases which had had surgical treatment. One patient was well six years after operation, another three years, and another one year. Three other cases were too recent for him to estimate the results. He believes that the prognosis can be predicted from the laboratory analysis.

Stewart and Copeland (5), in presenting a group of neurosarcomas, state that most fibrosarcomas can be placed under that heading. They feel that it is difficult to conclude what is the best form of treatment for these tumors. They were uniformly disappointed by the results of interstitial irradiation by buried radon implants. Certain tumors of low grade malignancy did well from the use of external irradiation above. In tumors of high grade malignancy, however, this type of therapy was very disappointing. In their opinion the dosage of external irradiation must be pushed to the point of sloughing of the normal tissues, and small dosage is of no avail in this fatal disease.

All of our cases had surgical excision of the lesion followed by radiation therapy. Of the 12 cases which we wish to report, seven patients are well at the present time, three have died of metastases, and two others died without evidence of metastases as the cause of death. Recurrence after operation developed in five cases—all are dead, but two did not die as a direct result of the tumor. In the seven cases in which recurrence did not develop, the patients are living and well at the present time.

One case (Case 1, below) had prompt recurrence, and under the influence of extensive roentgen therapy the tumor disappeared. There was marked muscular atrophy and skin changes as a result of the therapy. The patient died 11 years later from thrombosis of the brachial artery.

A second case, with a tumor primary in the lower leg, developed metastases in the spine, and radiotherapy was ineffectual, death following within a few months. A third case developed multiple metastases from a tumor of the thigh, one series of roentgen therapy was given post-operatively, but the patient died four years after operation. The fourth case (Case 2, below) developed local recurrence in the operative scar, and after extensive roentgen therapy developed pulmonary metastases and died five years after operation. The fifth case, a man aged 83 years, developed local recurrence in the forearm post-operatively. He had three series of roentgen therapy, but died three years later of general debility. There was still thickening present at the operative site.

Four cases were primary in the abdominal wall. These were all excised and post-operative roentgen therapy was applied. None of these patients developed any recurrence, and all are well at the present time. The time interval since the operation on these cases is eleven, eight, five, and five years, respectively. One other case was primary in the anterior chest wall. This was surgically excised and had post-operative roentgen therapy applied to it. This patient is living and well, with no recurrence, one year after operation.

Two cases originated in the extremities. One was primary in the heel and had metastatic glands in the groin. The primary tumor and the metastatic glands were excised and post-operative roentgen therapy was applied. The patient was well when

last heard of, more than a year later. The last case was a recent one, and no conclusions can be drawn. The tumor was excised from the thigh by means of the cautery and was then given post-operative roentgen therapy. This was a cellular type of tumor and appeared more malignant from the histologic picture than many of the others.

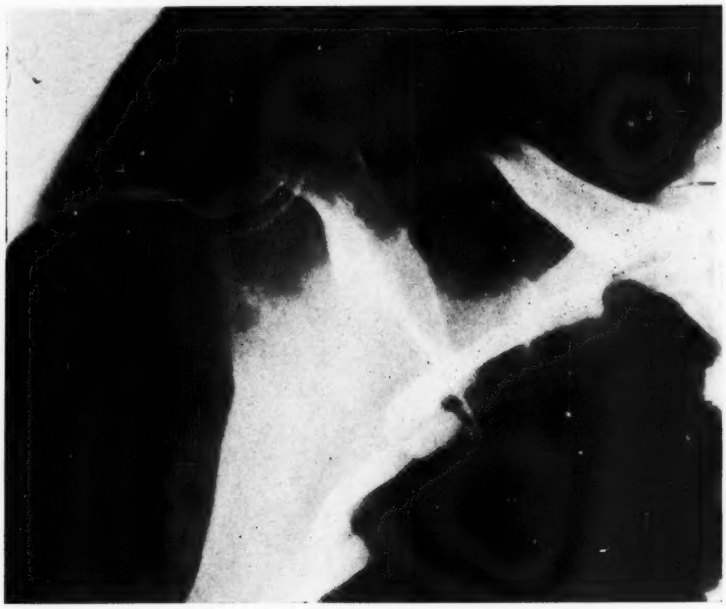

Fig. 1. Case 1.

CASE HISTORIES

Case 1. M. B., white female, 45 years of age. She came to the clinic in April, 1923, with the complaint of severe pain in the right shoulder, which had been developing gradually during the previous six months. At this time stiffness and impairment of function were present, also almost constant pain which interfered with sleep. A diagnosis of arthritis was made and physical therapy was advised. The patient was examined elsewhere, and a diagnosis of pressure symptoms from cervical ribs was arrived at. She was next seen in October, 1923. Examination disclosed evidence of a tumor mass in the axillary area, extending around to the scapula. It was quite hard, very tender to pressure, and about 6 cm. in diameter.

X-ray examination of the shoulder revealed a soft tissue tumor along the axillary border of the scapula just below the glenoid. There was no bone destruction. There was atrophy of disuse of all the bones in this area (Fig. 1).

At operation the tumor was found to be hard, fibrous, and encapsulated. It was adherent to the periosteum of the scapula and to the attachment of the latissimus dorsi muscle.

The pathological diagnosis was fibrosarcoma. It was thought to be a slowly growing, mildly malignant tumor of connective tissue origin.

Following the operation, one series of deep x-ray therapy was applied elsewhere—over the right axillary and scapular regions—a 110 per cent skin erythema dose being given.

The patient was seen again in June, 1924, at which time there was definite limitation of motion of the arm. X-ray ex-

amination showed an area of roughening along the axillary border of the scapula, suggesting the possibility of recurrence. After consultation with Dr. P. M. Hickey it was decided that inasmuch as this was a radioresistant, slow growing type of tumor,

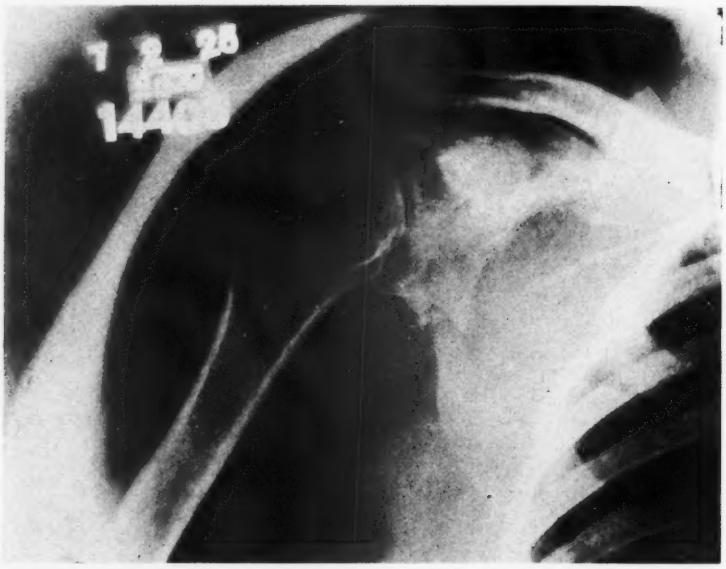

Fig. 2. Case 1.

Fig. 3. Case 1.

She was next seen in September, 1924, when a hard mass was felt along the anterior border of the scapula and another mass above the scapula.

X-ray therapy was started at that time. multiple small doses of x-ray therapy should be tried. Accordingly, the following factors were used: 190 kv., 50 cm. F.S.D., 0.5 mm. Cu + 1.0 mm. aluminum filtration, approximately 275 r units front and

back. This dosage was repeated weekly for four weeks, and after an interval of from four to six weeks the series was repeated. This routine was continued during the following 18 months.

The palpable tumor mass regressed and disappeared in two months. In April, 1925, x-ray evidence of recurrence along the anterior border of the scapula was apparent. In July, 1925, there was evidence of involvement of a large part of the body of the scapula, with fracture through the neck of the scapula (Fig. 2). Under continued x-ray therapy this remained stationary from that time. There was a moderate degree of pneumonitis along the axillary border of the lung, but this later disappeared.

After several years there developed a marked atrophy of the muscles of the shoulder and upper arm, with considerable telangiectasis of the skin over the treated area. There was also marked limitation of motion of the arm. In 1934 an ulcer formed over the point of the shoulder which resisted efforts to heal it (Fig. 3). In July, 1934, gangrene of the arm developed due to thrombosis of the brachial artery, and the patient died following amputation of the arm. No autopsy was permitted.

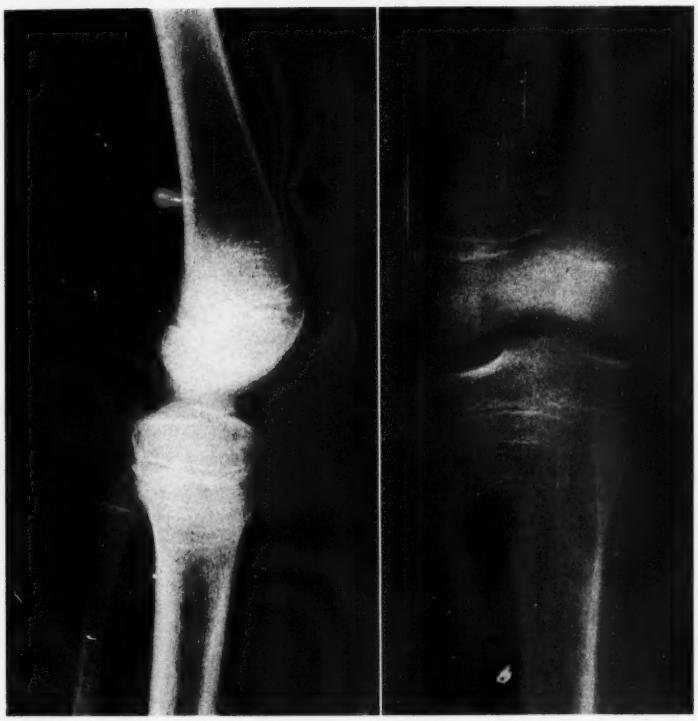

Fig. 4. Case 2.

Case 2. E. C., white male, 8 years of age. First seen in the clinic in September, 1930. At that time a history was obtained indicating that a tumor had been removed from the inner side of the left knee in another hospital during January, 1929. This recurred and had been again removed two weeks previous to the present admission. The tumor involved the soft tissues and apparently had no connection with the bone. The pathological diagnosis on each occasion had been fibrosarcoma.

Examination at that time revealed a moderately advanced flexion contracture and some thickening about the scar area. No other findings of interest were found.

X-ray therapy was administered as follows: Oct. 27, 1930, two portals (medial and lateral), 190 kv., 50 cm. F.S.D., 0.5 mm. copper and 1.0 mm. aluminum filtration, 550 r units. Similar doses were applied Dec. 30, 1930; March 14, 1931; May 26, 1931; Aug. 10, 1931, and Oct. 24, 1931. Post-operative x-ray therapy had also been applied before he was seen by us. The details are not available.

There was a gradual accumulation of fibrosis over the tumor area, but no definite tumor could be palpated. Some telangiectasis also developed in this area. The flexion contracture of the knee increased.

X-ray examination on admission showed no involvement of the bones of the knee by the tumor (Fig. 4).

X-ray examination of the knee on Dec. 15, 1932 (Fig. 5), showed evidence of eburnation around the epiphyseal lines and an unusual type of bone production which was perpendicular to the cortex of the femoral epiphysis. There was also a beginning dissolution of the epiphysis of the tibia along its medial margin. This deformity increased slightly, and on Jan. 6, 1934, the bone dissolution involved the medial portion of the diaphysis of the tibia just proximal to the epiphyseal line. The lungs were clear.

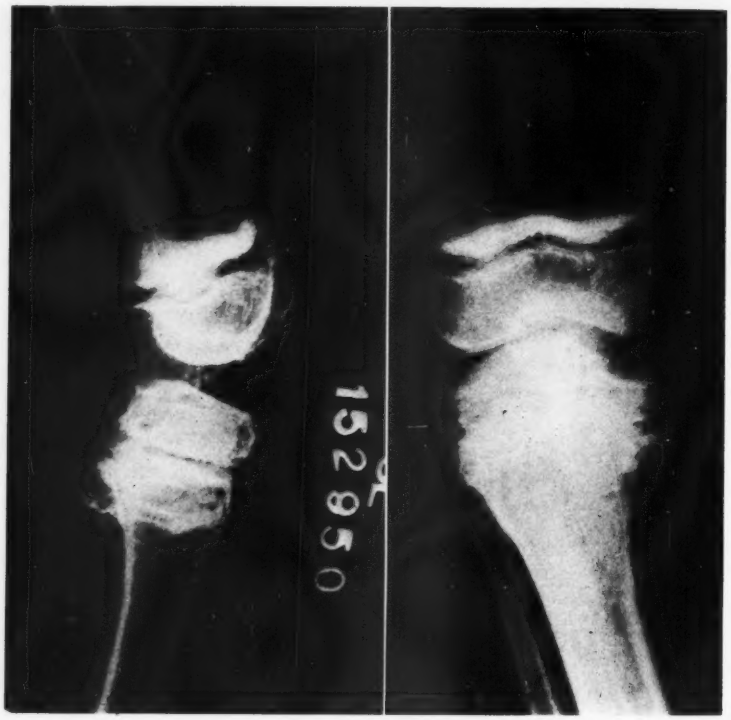

Fig. 5. Case 2.

On Aug. 16, 1934, the patient returned, stating that he fell while playing at school. X-ray examination revealed a fracture through the femur about two inches above the knee (Fig. 6). The abnormal bone changes had progressed very little. Callus

formed slowly at the site of fracture, but on Feb. 21, 1935, there was clinical evidence of union, and x-ray films showed a moderate amount of callus formation. The lungs were clear on May 1, 1935. During all this time constant effort was made to secure permission for amputation, but the family refused each time.

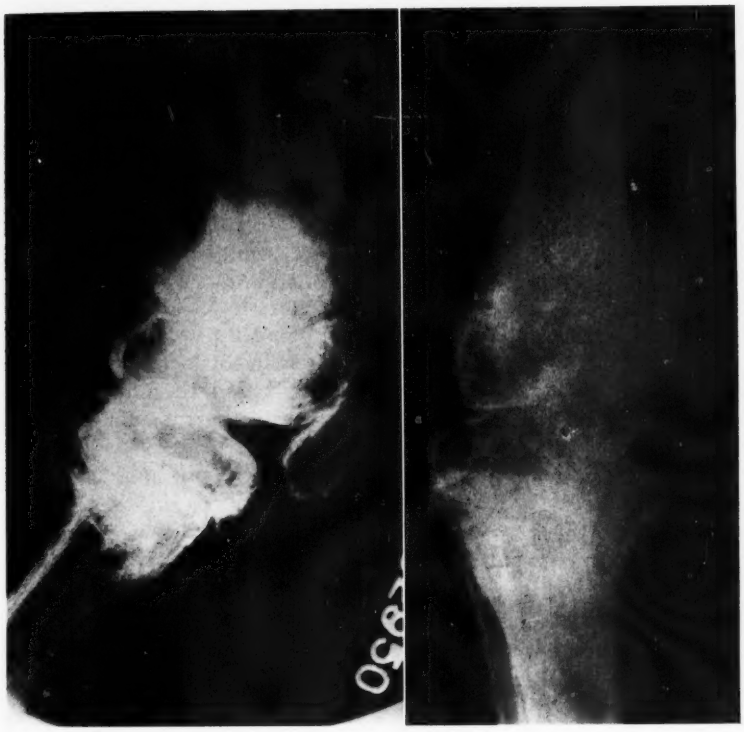

Fig. 6. Case 2.

During May the knee became swollen and gave every indication of recurrence of the malignancy. Biopsy confirmed the diagnosis.

X-ray films of the chest July 12, 1935, showed evidence of multiple areas of metastatic malignancy in both lungs. The patient expired Aug. 16, 1935.

DISCUSSION

It is difficult to arrive at definite conclusions from the study of a small series such as this, but when taken in conjunction with other similar studies one may obtain certain impressions which in themselves are of considerable value.

We have not attempted to go into the minute classification of tumors which might be included under this nomenclature. Certain authors believe that neurosarcomas constitute the majority of these tumors. There are other less well differentiated tumors which can be classified under the more inclusive term—fibrosarcoma. These are inclined to be less malignant and to metastasize less rapidly. When these tumors metastasize they do so through the blood stream, and the metastases are usually found in the lungs. One of our patients died of metastases to the lungs; one developed metastases in the spine, and one had multiple tumors over the body. Of the cases in the series of Quick and Cutler (3), 20 per cent metastasized to the lungs.

The prognosis in these tumors is not good, although here as in all other malignant tumors the stage of the disease is an important factor in estimating the probable outcome. Most authors believe that the most reliable prognostic sign is the histologic picture and that cases showing a high grade malignancy have an extremely high rate of mortality. In a large series such as that reported by Meyerding, Broders, and Hargrave (2) the five-year survival was in the neighborhood of 14 per cent. Stout (6) believes that in the very malignant type the survival will be less than 10 per cent regardless of the type of treatment used. Four of our cases died within five years, and one after eleven years. In two of these the tumor was not the cause of death.

It is difficult to appraise accurately the value of post-operative radiation therapy at this time, but it is our opinion that in those series in which this treatment has been liberally used the results show an improvement over straight surgical treatment. It is universally agreed that fibrosarcoma is a radioresistant tumor, but one is also favored by the fact that in a large number of cases the tumor remains localized for a considerable period, thus allowing sufficient time for the application of extended radiotherapy. With the newer methods of radiotherapy a much larger amount of radiation can be applied than formerly, and thus the problem of radioresistance is not so formidable as it once was.

In operable cases we recommend wide surgical excision, preferably by means of cautery, followed by prompt and vigorous roentgen therapy. Because of the lack of radiosensitivity the normal tissues cannot be spared and severe reactions may occur. Extensive muscular atrophy and telangiectasis of the skin sometimes occur, especially in cases in which an inoperable recurrence develops. In Case 1, reported here, such a recurrence developed, and under the influence of long continued radiation therapy marked atrophy of the muscles resulted as well as extensive telangiectasia. This soft tissue change was indirectly the cause of the patient's death 11 years later.

In cases in which the patient is in the growing age with unclosed epiphyseal lines, radiation therapy of any severity will frequently cause retardation of growth or even cartilaginous and bone fragmentation. A case of retardation of bone growth following roentgen therapy was reported several years ago by the man we are delighted to honor, Dr. Rollin H. Stevens (4). In our Case 2 the bone and joint changes were very striking. There was extensive dissolution of the devitalized bone and eventually fracture occurred from relatively light trauma.

We are, therefore, confronted by the dilemma of a persistent, fatal type of tumor, which in most instances is quite resistant to radiation therapy, situated in areas in which the surrounding and underlying tissues should be preserved if possible, and the fact that if sufficient radiation is applied to the tumor to cause its destruction these normal tissues will in all probability be irreparably damaged. We believe that if the facts can be fairly presented to the patient, little difficulty will be encountered in carrying out the necessary therapy.

SUMMARY

1. We are considering here fibrosarcoma of connective tissue origin. It is often a lesion of benign appearance and its serious import may not be known until the most favorable time for treatment has passed.

2. These tumors are essentially fibromatous in character, but their malignant nature is usually shown by evidence of invasion, mitosis, and anaplasia. The histologic picture is an excellent guide to the prognosis.

3. They may cause few symptoms, and these due to pressure. Roentgen examination will sometimes give assistance in outlining the tumor and in determining secondary bone changes.

4. The treatment consists of surgery and radiotherapy. The tumors are usu-

ally radioresistant and can be destroyed in many instances by extensive radiotherapy but, in so doing, considerable damage may be inflicted on the normal surrounding structures.

5. Twelve cases are presented, in all of which surgical excision was followed by roentgen therapy. Seven of these patients are living and well at the present time, three have died of metastases, and two others have died without evidence of malignancy as the cause of death.

6. Two case histories are presented. One patient lived 11 years after recurrence in the scapula, which recurrence was treated by roentgen therapy, with resulting extensive muscular atrophy and telangiectasia. Death occurred after amputation of the arm because of thrombosis of the brachial artery. The other patient had recurrence in the region of the knee and was treated by means of roentgen therapy. Death occurred five years later from pulmonary metastases. Interference in bone growth and bone dissolution occurred in the region of the epiphysis in this child.

7. Surgery, followed by adequate roentgen therapy, is advised, after warning the patient of possible damage to the normal structures.

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RADIOLOGICAL SOCIETIES IN THE UNITED STATES

CALENDAR

Meetings Falling Between the Dates of January 15 and February 28.

January 28, 29. Annual meeting of Conference of Eastern Radiologists, at the Warwick Hotel, 1701 Locust St., Philadelphia.

February 11, 12. Second annual conference of Mid-west Radiologists, Muehlebach Hotel, in Kansas City, Mo.

Editor's Note.—Will secretaries of societies please cooperate with the Editor by supplying him with information for this section.

CALIFORNIA

California Medical Association, Section on Radiology.—Chairman, John D. Lawson, M.D., 1306 California State Bldg., Sacramento; *Secretary,* Karl M. Bonoff, M.D., 1930 Wilshire Blvd., Los Angeles. Meets annually with California Medical Association.

Los Angeles County Medical Association, Radiological Section.—President, John F. Chapman, M.D., 65 N. Madison Ave., Pasadena; *Vice-president,* E. N. Liljedahl, M.D., 1241 Shatto St.; *Secretary,* Merl L. Pindell, M.D., 678 South Ferris Ave.; *Treasurer,* Henry Snure, M.D., 1414 Hope Street. Meets every second Wednesday of month at County Society Building.

Pacific Roentgen Club.—Chairman, Raymond G. Taylor, M.D., 1212 Shatto St., Los Angeles; *Secretary,* L. Henry Garland, M.D., 450 Sutter St., San Francisco.

COLORADO

Denver Radiological Club.—President, John S. Bouslog, M.D., 246 Metropolitan Bldg.; *Vice-president,* Sanford Withers, M.D., 304 Republic Bldg.; *Secretary,* Ernst A. Schmidt, M.D., Colorado General Hospital; *Treasurer,* H. P. Brandenburg, M.D., 155 Metropolitan Bldg. Meets third Tuesday of each month at homes of members.

CONNECTICUT

Connecticut State Medical Society, Section on Radiology.—Chairman, Kenneth K. Kinney, M.D., 29 North Street, Willimantic; *Vice-chairman,* Francis M. Dunn, M.D., 100 State Street, New London; *Secretary-Treasurer,* Max Climan, M.D., 242 Trumbull St., Hartford. Meetings twice annually in May and September.

DELAWARE

Affiliated with Philadelphia Roentgen Ray Society.

FLORIDA

Florida State Radiological Society.—President, Gerald Raap, M.D., 168 S. E. First St., Miami; *Vice-president,* H. O. Brown, M.D., 404 First Nat'l Bank Bldg., Tampa; *Secretary-Treasurer,* H. B. McEuen, M.D., 126 W. Adams St., Jacksonville.

GEORGIA

Georgia Radiological Society.—President, James J. Clark, M.D., Doctors Bldg., Atlanta; *Vice-president,* William F. Lake, M. D., Medical Arts Bldg., Atlanta; *Secretary-Treasurer,* Robert C. Pendergrass, M.D., Prather Clinic, Americus. Meetings twice annually, in November and at the annual meeting of the Medical Association of Georgia in the spring.

ILLINOIS

Chicago Roentgen Society.—President, David S. Beilin, M.D., 411 Garfield Ave.; *Vice-president,* Chester J. Challenger, M.D., 3117 Logan Blvd.; *Secretary-Treasurer,* Roe J. Maier, M.D., 7752 Halsted St. Meets second Thursday of each month, September to May, except December.

Illinois Radiological Society.—President, Ivan Brouse, M.D., 316 W. State, Jacksonville; *Vice-president,* Cesar Gianturco, M.D., Carle Hospital Clinic, Urbana; *Secretary-Treasurer,* Edmund P. Halley, M.D., 968 Citizens Bldg., Decatur. Meetings quarterly by announcement.

Illinois State Medical Society, Section of Radiology.—President, Roswell T. Pettit, M.D., 728 Columbus St., Ottawa; *Secretary,* Ralph G. Willy, M.D., 1138 N. Leavitt St., Chicago.

INDIANA

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IOWA

The Iowa X-ray Club.—Holds luncheon and business meeting during annual session of Iowa State Medical Society.

MAINE

See New England Roentgen Ray Society.

MARYLAND

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MASSACHUSETTS

See New England Roentgen Ray Society.

MICHIGAN

Detroit X-ray and Radium Society.—President, C. C. Birkelo, M.D., Herman Keifer Hospital; *Vice-presi-*

dent, E. W. Hall, M.D., 10 Peterboro St.; *Secretary-Treasurer*, E. R. Witwer, M.D., Harper Hospital. Meetings first Thursday of each month from October to May, inclusive, at Wayne County Medical Society Bldg.

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NEW HAMPSHIRE

See New England Roentgen Ray Society.

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OHIO

Cleveland Radiological Society.—President, North W. Shetter, M.D., Lakewood City Hospital, Lakewood; *Vice-president*, John Heberding, M.D., St. Eliza-

beth's Hospital, Youngstown; *Secretary-Treasurer*, Harry Hauser, M.D., Cleveland City Hospital, Cleveland. Meetings at 6:30 P.M. at Cleveland Chamber of Commerce Club on fourth Monday of each month from October to April, inclusive.

Radiological Society of the Academy of Medicine (Cincinnati Roentgenologists).—*President*, George Benzing, M.D., St. Elizabeth Hospital, Covington, Ky.; *Secretary-Treasurer*, Justin E. McCarthy, M.D., 707 Race St., Cincinnati, Ohio. Meetings held third Tuesday of each month.

PENNSYLVANIA

Pennsylvania Radiological Society.—President, Sydney J. Hawley, M.D., Geisinger Memorial Hospital Danville; *First Vice-president*, William J. McGregor, M.D., 744 Franklin Ave., Wilkinsburg; *Second Vice-president*, Oscar M. Weaver, M.D., 12 S. Main St., Lewistown; *Secretary-Treasurer*, Lloyd E. Wurster, M.D., 416 Pine St., Williamsport; *President-elect*, Charles S. Caldwell, M.D., 520 S. Aiken Ave., Pittsburgh. Annual meeting, May, 1938. Exact date and place to be decided.

Philadelphia Roentgen Ray Society.—President, Thomas P. Laughery, M.D., Germantown Hospital; *Vice-president*, Elwood E. Downs, M.D., Jeans Hospital, Fox Chase; *Secretary*, Barton H. Young, M.D., Temple University Hospital; *Treasurer*, R. Manges Smith, M.D., Jefferson Hospital. Meetings first Thursday of each month from October to May, Thompson Hall, College of Physicians, 19 S. 22nd St., 8:15 P.M.

The Pittsburgh Roentgen Society.—President, F. L. Schumacher, M.D., Jenkins Arcade; *Secretary*, H. N. Mawhinney, M.D., Mercy Hospital. Two Fall and two Spring meetings at time and place designated by president.

RHODE ISLAND

See New England Roentgen Ray Society.

SOUTH CAROLINA

South Carolina X-ray Society.—President, Robert B. Taft, M.D., 105 Rutledge Ave., Charleston; *Secretary-Treasurer*, Hillyer Rudisill, M.D., Roper Hospital, Charleston. Meetings in Charleston on first Thursday in November, also at time and place of South Carolina State Medical Association.

SOUTH DAKOTA

Meets with Minnesota Radiological Society.

TENNESSEE

Memphis Roentgen Club.—Chairmanship rotates monthly in alphabetical order. Meetings second Tuesday of each month at University Center.

Tennessee State Radiological Society.—President, H. S. Shoulders, M.D., 246 Doctors Bldg., Nashville; *Vice-president*, S. S. Marchbanks, M.D., 508 Medical Arts Bldg., Chattanooga; *Secretary-Treasurer*, Franklin B. Bogart, M.D., 311 Medical Arts Bldg., Chattanooga. Meeting annually with State Medical Society in April.

VERMONT

See New England Roentgen Ray Society.

VIRGINIA

Radiological Society of Virginia.—President, Fred M. Hodges, M.D., 100 W. Franklin St., Richmond; *Vice-president*, L. F. Magruder, M.D., Raleigh and College Aves., Norfolk; *Secretary*, V. W. Archer, M.D., University of Virginia Hospital, Charlottesville.

WASHINGTON

Washington State Radiological Society.—President, H. E. Nichols, M.D., Stimson Bldg., Seattle; *Secretary*, T. T. Dawson, M.D., Fourth and Pike Bldg., Seattle. Meetings fourth Monday of each month at College Club.

WISCONSIN

Milwaukee Roentgen Ray Society.—Secretary, S. A. Morton, M.D., Columbia Hospital, Milwaukee. Meets monthly on first Friday.

Radiological Section of the Wisconsin State Medical Society.—Secretary, Russel F. Wilson, M.D., Beloit Municipal Hospital, Beloit. Two-day annual meeting in May and one day in connection with annual meeting of State Medical Society, in September.

University of Wisconsin Radiological Conference.—Secretary, E. A. Pohle, M.D., 1300 University Ave., Madison, Wis. Meets every Thursday from 4 to 5 P.M., Room 301, Service Memorial Institute.

News Item

The Georgia Radiological Society was organized at the Palmer House, Chicago, during the Fifth International Congress of Radiology. The first regular meeting was held in Atlanta, Ga., Nov. 27, at the Academy of Medicine. The program consisted of a round table discussion of difficult diagnostic cases and of therapy problems. Fifteen men were present. A constitution and by-laws were adopted and plans made for the next meeting in conjunction with the Medical Association of Georgia at Augusta, next spring. The meeting was followed by a luncheon at the Biltmore Hotel.

EDITORIAL

LEON J. MENVILLE, M.D., *Editor* HOWARD P. DOUB, M.D., *Associate Editor*

THE EVOLUTION OF RADIOLOGY

A TRIBUTE TO DR. ROLLIN H. STEVENS, ONE OF AMERICA'S OUTSTANDING PIONEERS IN THIS SCIENCE

IT seems but yesterday that Röntgen's epochal discovery was flashed to the world and so, to those who were fortunate enough at that time to be on their way toward a medical career, congratulations are extended. And, when certain professional men have been still further favored by living through the intervening period and have been permitted to extend a guiding hand toward shaping the destinies of x-ray energy, that, too, may well be considered a fortuitous opportunity which is accorded to relatively few. One of those fortunate few is our own distinguished honoree, Dr. Rollin H. Stevens.

Let us look back for a moment to those stirring days in the late nineties when Röntgen's achievement startled the world. Let us recall to mind the press notices, the skepticism, the condemnation, the enthusiasm, the ridicule, the warnings, and in fact the entire potpourri of emotional misinformation which, sad to relate, still crops out from time to time despite over forty years of study and education through all the world's scientific channels of learning. Would that time permitted a review of all the points gained, all the suffering endured, all the difficulties overcome, all the disappointments, the hopes, the expenses; tersely, the total cost in human energy, endurance, and even death. And all this in order that the energy of radiation might be made useful and safe in the diagnosis, treatment, and cure of human disease. Now, at long last, the medical profession, through its radiological members, has won the battle against ignorance and prejudice, and has placed the science of radiology upon its proper accredited plane.

Undoubtedly a number of Dr. Stevens' friends will contribute richly to our fund of scientific information in this splendid issue, so the writer will present only one controversial point—the problem of filtration. While still a medical student he had opportunity to come in contact with therapeutic radiation during its earliest experimental stages. Among those early memories is a distinct recollection of purchasing a can of white lead in oil and painting our tubes white with a small circular window opening directly over the anodal point of x-ray emergence. This was for "protection." Memory, however, is not very clear as to the early filters, although I seem to recall that filters of any kind were not used until 1897 or 1898. Anyway, it is certain that filtration was pure guess-work like every other factor involved in early radiation therapy, but as experience has accumulated I have become convinced that unfiltered or raw radiation has no place in modern medical practice. By radiation in this sense is meant x-rays and radium.

There are naturally those who take an opposite viewpoint. Nevertheless, when one meets, all too frequently, with numerous cases of superficial malignant disease conditions treated by fractional doses of semi-filtered or unfiltered x-rays or radium (and in the hands of competent men, too)

and finds, as a result, that further radiation treatment is futile, the general subject of filtration offers a broad field for discussion. There may be good reasons, theoretical or otherwise, for the use of unfiltered radiation but when such treatment is given in connection with neoplastic disease affecting not only the skin but all structures immediately underneath, there seems to be no plausible reason for its use. Therefore, based upon my own experience in the use of both x-rays and radium up to their new high levels of short wave output, I desire to go on record as voicing my unqualified opposition to the use of unfiltered x-rays or radium containers for any human ailment or for the treatment of any disease. This statement is not given by virtue of any enthusiastic impulse but is based solely upon our daily experience and observation during a lifetime service with radiation therapy.

Whether this expression of opinion finds favor in the eyes of our honored friend Rollin Stevens, I do not know. I do know, however, that the energy of radiation will remain young over many centuries to come, like our own Dr. Stevens, who has remained young and virile and will continue to do so to the end.

Dr. Stevens has contributed much of his own forceful and pleasing personality to each and every phase of radiological progress; he has lent a guiding hand in correcting abuses in radiation therapy; he has become an authority on therapeutic radiology, and particularly that branch dealing with skin and superficial disease; he has been instrumental in placing this important branch of medical practice upon the highest professional plane—Dr. Stevens, whose virile manhood and staunch Americanism have been an inspiration to all who have been fortunate enough to know him as a teacher and a man. To you, Dr. Stevens, may I be permitted to inscribe these lines in grateful memory of many profitable and delightful hours spent in your congenial company. Rollin, time has been kind to you. It has permitted you to reach the honorable age of three score and ten in full possession of your mental and physical vigor. May you continue on in the pursuit of your work and play, and may you find at every port of call a snug harbor and a cozy berth. God bless you!

ALBERT SOILAND, M.D.

ANNOUNCEMENTS

FURTHER HONORS FOR A MEMBER OF THE SOCIETY

Dr. Francis Carter Wood, Director of the Institute of Cancer Research, Columbia University, and Editor of the "Journal of Cancer," has been decorated with Belgium's Order of the Crown. King Leopold III conferred the honor upon Dr. Wood in recognition of the latter's research work in cancer control.

Dr. Wood is a past-president of the Radiological Society of North America, and to his constructive work while President the Society owes much of its present success. His friends congratulate him and all radiologists can well feel gratification in each new honor that comes to Dr. Wood, knowing that it is truly earned.

ROYAL SOCIETY OF EDINBURGH

A David Anderson-Berry Gold Medal, together with a sum of money amounting to about £100, will be awarded in July, 1938, by the Royal Society of Edinburgh to the person who, in the opinion of the Council, has recently produced the best work on the nature of x-rays in their therapeutic effect on human diseases. A similar award will be made every three years.

Applications for this prize are invited. They may be based on both published and unpublished work and should be accompanied by copies of the relevant papers.

Applications must be in the hands of the General Secretary, Royal Society of Edinburgh, 22 George Street, Edinburgh, 2, by *June 1, 1938.*

This announcement was first published in the March, 1937, issue of RADIOLOGY, page 373, and is here repeated by request.

IN MEMORIAM

WILBUR S. WERNER

Mr. Wilbur S. Werner, well known to many members of the Radiological Society of North America as president of the Kelley-Koett X-

ray Company, passed away in Minneapolis, December 16, 1937. He had recently suffered from a rather severe sinus infection, and went to Florida to convalesce. Feeling that the completion of a new high voltage installation in Saint Paul demanded his attention, he made the trip, unwisely, as events proved. December 11 he was taken to the hospital with Type 3 lobar pneumonia, from which he succumbed.

Mr. Werner has always been a close friend of this Society, and many radiologists will be saddened to hear of his passing. A close tie must of necessity exist between makers and users of roentgen apparatus, and Mr. Werner was always counted one of us.

BOOKS RECEIVED

Books received are acknowledged under this heading, and such notice may be regarded as an acknowledgment of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

LA HERNIE POSTERIEURE DU MENISQUE INTERVERTEBRAL (HERNIE NUCLEAIRE POSTERIEURE), ET SES COMPLICATIONS NERVEUSES. By PIERRE GLORIEUX. A volume of 102 pages, with 98 illustrations. Published by Masson et Cie, Paris, 1937. Price: 40 fr.

PRIMARY CARCINOMA OF THE LUNG. By EDWIN J. SIMONS, M.D., with Foreword by J. ARTHUR MYERS, M.D., Professor of Medicine and Preventive Medicine and Public Health, University of Minnesota; President National Tuberculosis Association. A volume of 263 pages, with 30 illustrations. Published by Year Book Publishers, Chicago, 1937. Price: $5.00.

ATLAS OF SKELETAL MATURATION. By T. WINGATE TODD, M.B., Ch.B. (Manc.); F.R.C.S. (Eng.). A volume of 202 pages, with 35 illustrations. Published by the C. V. Mosby Company, St. Louis, 1937. Price: $7.50.

BOOK REVIEWS

ARTIFICIAL FEVER PRODUCED BY PHYSICAL MEANS: ITS DEVELOPMENT AND APPLICATION. By CLARENCE A. NEYMANN, A.B., B.S., F.R.S.M., Associate Professor Psychiatry, Northwestern University Medical School; Honorary Professor of Medicine, National University of Mexico; C.R.B., Exchange Professor of the University of Ghent, Liege, Louvain, and Brussels, Belgium. A volume of 293 pages, with 68 illustrations and 4 colored plates. Published by Charles C. Thomas, Springfield, Illinois, 1937. Price: $6.00.

To my knowledge this is the first textbook on this subject. It contains fifteen chapters covering in order the history, physiology, technic, and application in various clinical conditions. The subject matter is clear and concise and gives an excellent description of the various methods of producing artificial fever. The various methods of producing artificial fever are described briefly and the apparatus for each method are shown clearly in several figures. The chapters on the clinical application of artificial fever recite the results obtained by many workers as well as those of the author. The book is particularly advantageous because of its extensive bibliography in which some 556 references are listed.

I believe this book will be of great value to anyone interested in the use of artificial fever since it is a good résumé of the work carried on in the production of fever by artificial means by the author and other outstanding workers in this field of medicine.

L'ARTERIOGRAPHIE DES MEMBRES ET DE L'AORTE ABDOMINALE: ÉTUDE CRITIQUE. By HENRY REBOUL. A volume of 136 pages, with 81 illustrations. Published by Masson et Cie, 1935. Price: 40 fr.

This monograph is a fairly comprehensive and definitely enthusiastic treatise on the subject of arteriography and its possibilities. The author reviews the literature and discusses the various types of contrast media which have been used. His experience is based on 218 injections for arteriography, given to 140 patients. He devotes one chapter to accidents and untoward results. His technic is for the most part that of Dos Santos. He uses transcutaneous arterial puncture under general anesthesia and injects the medium under a mechanical pressure of from 1 to 1.5 kg. He abandoned thorotrast as a contrast medium chiefly because of its retention in the body and because of the question of its radio-activity. He used for the majority of his arteriograms a 45 per cent solution of "Tenebryl," sodium diiodomethane sulphonate, and gives reasons why he feels that this is superior to other iodides. The 81 illustrations are for the most part good arteriograms but their impressive-

ness is weakened by the appearance of their having been obviously retouched. The plates are accompanied by good, short abstracts of histories. Many pictures are shown which illustrate various typical features of senile and presenile arteritis (arteriosclerosis obliterans), although very few show the lower portion of the leg and the foot. Only two cases of thrombo-angiitis obliterans are illustrated and these do not emphasize the typical arteriographic findings in this disease. Only one arteriogram of a patient with Raynaud's disease is shown and this is reduced too much to show the digital arteries. There are several good plates of arterial aneurysm and one of an arteriovenous fistula. The author also attempts to show distinguishing arteriographic findings in association with certain bone tumors. Four arteriograms of the abdomen, taken after injection into the aorta, are shown. The author feels that arteriography gives valuable information regarding confirmation of the clinical diagnosis of arterial diseases and regarding the extent and localization of arterial occlusions, of parietal arterial lesions, and of tumors and lesions of the bones of the extremities.

SYNOPSIS OF DIGESTIVE DISEASES. By JOHN L. KANTOR, Ph.D., M.D., Associate in Medicine, Columbia University; Gastro-enterologist and Associate Roentgenologist, Montefiore Hospital for Chronic Diseases, New York. A volume of 302 pages, with 40 illustrations. Published by the C. V. Mosby Company, St. Louis, Missouri, 1937. Price: $3.50.

The object of Kantor's book, according to the preface, is "to present simply, clearly, and concisely the essential facts concerning the diseases of digestion." It is obviously extremely difficult to accomplish this purpose in 286 pages, and there naturally will be certain shortcomings in that it is impossible to give to individual diseases which are important the space they require to properly bring out factors of importance. The book is an attractive one which is arranged artistically. The division of the material included is done in an orderly manner.

The book is divided into four parts, the first dealing with the classification of digestive disorders, diagnostic and therapeutic methods, and a discussion of constitutional inferiority, and gastro-intestinal allergy. In the second portion is a discussion of disease which includes the biliary system as well as every portion of the intestinal tube from the mouth to the anus. All of these diseases are covered in 184 pages, a formidable task indeed, but one which Kantor accomplishes with a surprising degree of completeness. Part III includes a consideration of digestive symptoms and extra-digestive diseases. This part is hung on as a sort of suffix and could be done with more completeness. Kantor's book is one which because of its completeness, attractive editing, and orderliness should appeal to any physician who has any interest whatsoever in the digestive tract.

DIE BIOLOGISCHE BEDEUTUNG DER INFRAROTEN STRAHLEN (The Biologic Significance of Infra-red Rays). Also Supplement 1 of Volume 4 (1937) of Helvetica Medica Acta. By O. MERKELBACH. A volume of 64 pages, with 29 illustrations. Published by Benno Schwabe & Company, Basel, 1937. Price: Swiss Fr. 4.00

A critical review of the literature dealing with the biologic effect of infra-red rays convinced the author that very little reliable information exists and that, above all, the fundamental physical data are entirely lacking. He studied, therefore, especially the infra-red spectra of a number of compounds, beginning with water, chloroform, alcohol, amino acids and ending up with hemoglobin, its derivatives and also chlorophyll. The methods employed are described and the advantages and disadvantages of thermo-spectrography and photospectrography discussed. The results of the experiments seem to indicate that infra-red rays of 0.76–1.0 m. may produce biologic effects in connection with local or systemic sensitization. A short chapter dealing with infra-red photography is included.

The study of this monograph must be considered a necessity by all those who wish to investigate the clinical aspect of infra-red therapy.

SOME QUANTITATIVE ASPECTS OF THE BIOLOGICAL ACTION OF X- AND GAMMA-RAYS. By C. M. SCOTT, M.D., issued by Medical Research Council, Special Report Series No. 223, London, 1937. A volume of 99 pages. Price: 1 shilling, 6 pence.

This short monograph in pamphlet form is divided into two parts. In the first portion the author briefly summarizes and analyzes the

evidence bearing on the mechanism involved in the action of roentgen rays and the gamma rays of radium on living tissue. The second portion is devoted to a report of experiments carried out by the author to elucidate obscure phases of the action of roentgen rays and radium on certain tissues, especially the muscular tissues of the heart which are known to be resistant to irradiation, and on the eggs of the Blue Bottle fly which are distinctly sensitive to irradiation. In the experiments on the Blue Bottle fly the author investigated the effect of varying the intensity of irradiation, the effect of the changes in the rate of development of the eggs during irradiation as affected by temperature, by injury, and by irradiation, separately or combined; the effect on radiosensitiveness of injury produced by asphyxia or injury produced by x-rays or both; the effect on radiosensitiveness of anesthesia such as chloroform, nitrous oxide, ether, and certain fat solvents such as petrol ether, by themselves or in combination with roentgen irradiation.

The first portion of this brief monograph in which the author discusses and analyzes the evidence bearing on the action of roentgen rays and the gamma rays of radium on living tissue is perhaps the best effort of the kind with which the reviewer is familiar. The author is to be highly complimented on his ability to set forth the experimental work which has already been done and to analyze it clearly and soundly. This monograph should be read by everyone who wishes to know and to understand as much as possible about the action of roentgen rays and the gamma rays of radium on living cells.

MORPHOLOGISCHEN UND TIEREXPERIMENTELLE STUDIEN ÜBER DAS SCHLEIMHAUTRELIEF DES MAGEN-DARMKANALS. Beitrag zur Kenntnis der anatomischen Unterlage des Schleimhautreliefs und des Mechanismus der Faltenbildung. By STEN GRETTVE, M.D. Acta Radiologica, Supplementum XXXI. Published by P. A. Norstedt & Son, Stockholm, 1936. A volume of 124 pages, with 43 illustrations. Price: 10 Sw. cr.

The author investigates in morphological and pharmacological studies, together with animal experiments, the mucosa relief of the gastro-intestinal tract and continues Forssell's work concerning the autoplastic of the gastric mucosa. He concludes that the formation of folds is due to an active creative power of the muscularis mucosæ and muscularis propriæ, shaped according to its need of digestion. These studies complete also O. Dye's and W. Knothe's pharmacological experiments in regard to mucosa changes in man and reflect Chaoul's doctrine of the preformation of the mucosal folds. As to the practical clinical side of the study, it constitutes an important contribution, especially for the evaluation of inflammatory changes of the gastro-intestinal mucosa.

THE COLLAPSE THERAPY OF PULMONARY TUBERCULOSIS. By JOHN ALEXANDER, M.D., F.A.C.S., Professor of Surgery, University of Michigan; Surgeon-in-Charge, Division of Thoracic Surgery, Department of Surgery, University of Michigan Hospital. A volume of 705 pages, with 367 illustrations. Published by Charles C. Thomas, Springfield, Illinois, 1937. Price: $15.00.

Twelve years ago, when "The Surgery of Pulmonary Tuberculosis" was published, treatment of tuberculosis consisted of a regimen in which general physical and pulmonary rest were obtained and continued over an indeterminate period of years. Sanatoriums were filled with patients who had advanced fibroid tuberculosis and who continued vain efforts to regain health and return to work. Surgical methods, with the exception of infrequent induction of collapse of the lung by pneumothorax, were looked on with suspicion. Alexander's fine work brought about gradually a complete reversal of practice. Other important works also contributed to that end, so that now many large sanatoriums find that 75 per cent of their patients are suitable for one or more types of surgical treatment.

In the present work, Alexander and his coworkers have enlarged the scope of the first book to such extent that they are able to assemble in one volume a discussion of all methods accepted as valuable in treatment of tuberculosis. Any student can find, either in the content of this work or in the works referred to in the bibliography, all that is at present known about treatment of the patient who has tuberculosis. Twelve years ago there were 500 references in the bibliography: now there are 1,342 articles and books whose authors express the views taught in all parts of the world. Of these, Alexander has contributed thirty-four of his personal publications. One cannot overestimate the importance of the chapter, containing thirty-eight pages, that deals with the

bibliography. Without this essential chapter the book would lose much of its importance as a great book of reference.

The student will find that the chapter entitled "Physiological Principles of Collapse Therapy" will help in understanding the responses of lung following operation, and especially the compensatory mechanisms brought into play when the lung is reduced in volume by collapse. The physiologic responses to each variety of condition are described separately and include such effects as those of muscular compensation, effects on the circulation, changes in flow of lymph, the occurrence and significance of air embolism and pleural effusion, and the extent of respiratory embarrassment incidental to decrease of vital capacity.

The indications for each type of operation employed in bringing about and maintaining satisfactory collapse are discussed in a separate chapter. As a supplement there is added a reference guide consisting of eighty-four diagrams representing the principal types of pulmonary and pleural lesions for which collapse therapy may be used. Each legend indicates briefly the operation or sequence of operations to be used in treatment.

In descriptions of both minor and major operations, great care is taken in describing, not only the operative technic, but pre-operative preparation, accidents that may be encountered, and the most approved methods of combating them. Post-operative management meets with an equally careful consideration and, finally, the results obtained from each method of operative attack are discussed frankly.

Physicians will welcome this book because of the help given in the discussion of physiologic effects entailed and the statistical evidence of the value of the several methods of treatment. Surgeons will welcome it for the same reasons, but, in addition, will find it of greatest service not only in forming conclusions with reference to choice of operations in particular cases, but also in the guidance in technic suggested.

Perhaps the book might be criticized because of size rather than content. Yet it is difficult to choose the subject matter that might be deleted and still have what it is designed to be: a book of reference for students of tuberculosis.

RADIATION THERAPY: Its Use in the Treatment of Benign and Malignant Conditions. By IRA I. KAPLAN, M.D., Clinical Professor of Surgery, New York University Medical College; Director, Radiation Therapy Department, Bellevue Hospital, New York; Director, Division of Cancer, Department Hospitals, City of New York; Director, New York City Cancer Institute; Associate Radiologist, Lenox Hill Hospital, New York; Editor (Therapeutic Section) "Year Book of Radiology." A volume of 558 pages, with 198 illustrations. Published by the Oxford University Press, New York City, 1937. Price: $10.00.

One could guess that a text on radiotherapy written by one with Kaplan's experience and knowledge of the world's literature would be an outstanding one. It is, and Kaplan deserves sincere congratulations for so ably handling the vast subject of radiotherapy. Although the book is written for students and practitioners, the radiotherapeutist will do well to look it over as a "refresher." Of course, one could find fault with some details such as the length of the presentation of gynecologic and the brevity of the consideration of inflammatory and neurologic lesions, but Kaplan decided on this allotment of space after far more thought than this reviewer used in this criticism. Many things recommend the book, its whole set-up, the illustrations, the index, the omission of statistics and voluminous literature, and especially the presentation of the treatment of oral, mammary, uterine, and rectal carcinomas. Braestrup is to be particularly commended for his chapter on the Physics of Radiation.

ABSTRACTS OF CURRENT LITERATURE

CONTENTS BY SUBJECT

THE FOLLOWING ABSTRACTORS HAVE CONTRIBUTED TO THIS ISSUE

S. M. Atkins, M.D., of Waterbury, Conn.
S. Richard Beatty, M.D., of Madison, Wis.
G. E. Burch, M.D., of New Orleans, La.
J. E. Habbe, M.D., of Milwaukee, Wis.
Lewis G. Jacobs, M.D., of Madison, Wis.
Ernst A. Pohle, M.D., Ph.D., of Madison, Wis.
W. A. Sodeman, M.D., of New Orleans, La.

ABSTRACTS IN THIS ISSUE LISTED ALPHABETICALLY BY AUTHORS

ANIMAL EXPERIMENTATION

Radiation Injury of the Sperma of Mice and Rats as Observed on the Early Development of the Ova. H. Brenneke. Strahlentherapie, 1937, **60,** 214.

The testicles of adult mice and rats were irradiated with roentgen rays; 800–2,200 r were given to mice and 800–1,800 r to rats. The effect on the mature sperm cells was studied by observing the impregnated ova of female animals. It appeared that the fertility of the sperma stored in the epididymis is not influenced by irradiation. The percentage of non-impregnated ova was 7.39 per cent for mice and 5.25 per cent for rats. The fertile period of the mouse after irradiation lasts approximately two weeks regardless of the dose applied. Some of the impregnated ova showed abnormal development and in some cases abortion occurred. There was a definite difference in the susceptibility of the two types of animals because, following irradiation with 800 r, 80 per cent of the ova of rats and only 65 per cent of the ova of mice showed normal development. In conclusion, the author warns again against indiscriminate exposure of the generative organs in man.

ERNST A. POHLE, M.D., Ph.D.

Experimental Contribution to the Problem of the Time Factor. H. Kirchhoff and W. Kelbling. Strahlentherapie, 1937, **60,** 444.

The authors exposed the testicles of 14 adult rabbits; one was treated by fractional doses, the other by protracted fractional doses. Technic: 170 kv., 1.2 mm. Cu + 1 mm. Al and 180 kv., 0.7 mm. Cu + 1 mm. Al. The focal skin distances were 20 and 125 cm. The single doses 200 r (in air) were given at intervals of 24 hours. In a few instances single doses of 30, 40, and 50 r were used while the total dose varied from 300 to 1,800 r. This allowed a ratio in the r/min. from 1:5.5–1:39. The animals were killed from four to 43 days after the last exposure. Careful histological examinations of the testicles treated with both methods showed that the effect of the protracted fractional irradiation was not greater than that of the simple fractional dose method. It is emphasized, however, that these results which have been obtained on normal tissue may not be transferred to malignant tumors in humans.

ERNST A. POHLE, M.D., Ph.D.

ARTERIOGRAPHY

Diagnostic and Therapeutic Relation of Arteriography. R. Demel and M. Sgalitzer. Wien. klin. Wchnschr., May 7, 1937, **50,** 595, 596. (Reprinted by permission from British Med. Jour., June 26, 1937, p. 103 of Epitome of Current Medical Literature.)

The authors stress the therapeutic value of arteriography in cases of endarteritis obliterans, Raynaud's disease, arteriosclerosis, thrombosis, etc., apart from the important diagnostic value of the method. In a number of cases they were able to observe a remarkable improvement in the condition of the limb following an intra-arterial injection of 20 c.c. of a 20 per cent solution of perabrodil. They explain the favorable therapeutic result by a persistent dilatation of the arterioles following the injection. The injection can be repeated after some time if necessary.

BIOLOGIC EXPERIMENTATION

The Biologic Effect of Continuous and Periodically Interrupted Roentgen Irradiation upon the Eggs of the Fruit Fly. A. Gregori. Strahlentherapie, 1937, **60,** 422.

The author compared the biologic effect of roentgen rays on the eggs of the fruit fly if they were applied either in the form of a continuous exposure or by periodically interrupted exposures. Technic: 180 kv., 15 ma., 0.35 mm. Cu + 0.5 mm. Al, 6–417 r/min. By means of a rotating disc the interrupted exposures gave doses equal to the continuous exposure of 50 and $2^1/_2$ seconds from 180 to 5 seconds. The experiments showed that by decreasing the number of r per minute for continuous exposure the biologic effect is definitely decreased. If the eggs were irradiated with a high number of r/second, at the same time increasing the time of exposure without changing the doses by means of periodical interruptions of the irradiation, the biologic effect was not the same as that obtained with continuous exposure during the same time. It could be demonstrated that in such case it was greater and corresponded to the effect produced with continuous irradiation and a high number of r/min. The experiments were carried out with the ratio of 1:3 between intensity and time.

ERNST A. POHLE, M.D., Ph.D.

THE BLOOD

The Effect of Radium and of Benzol on the Blood and Blood-forming Organs, with Special Consideration of the Leukocytes. A. Feller. Strahlentherapie, 1937, **60,** 393.

The author studied the toxic effect of radium and benzol on the blood and blood-forming organs in rats. Both produce changes in the total number and the percentage distribution of leukocytes. These changes as well as the histological findings in the various organs were very similar following radium exposure and benzol administration. However, regeneration set in much earlier following benzol as compared with radium. So far it is impossible to determine whether or not the observed changes are due to a direct effect of benzol and radium on the leukocytes or due indirectly to an injury of the blood-forming organs.

ERNST A. POHLE, M.D., Ph.D.

BONE DISEASES (DIAGNOSIS)

Non-specific Osteitis of the Ribs. Kåre T. Poulsson. Acta Radiologica, August, 1937, **18,** 643–651.

Osteitis of the ribs occurs principally as two chronic specific infections, tuberculosis and syphilis. Of these

two, tuberculous osteitis of the ribs is by far more common, the syphilitic type being seldom encountered. Acute, specific infectious osteitis of the ribs is seen in typhus and febris undularis. Non-specific, metastatic osteitis of the ribs is regarded as a very rare affliction, accounting for 0.8 to 2 per cent of all cases of osteomyelitis recorded. Non-specific osteitis of the ribs occurs in young individuals. There is probably a six-month interval between the appearance of the primary infection and metastasis to the ribs. In individuals in the growing period the disease is almost always acute with definite local as well as general symptoms and a tendency to rapid destruction with suppuration and formation of fistulæ. In individuals over 25 years of age, the clinical picture is quite different; the symptoms develop slowly and the condition runs a chronic course. Local and constitutional symptoms are mild. Occasionally there are no symptoms and the osteitis of the rib is accidentally discovered. These findings are said to be due to the poor vascularization of the ribs after the age of 25 years. *Staphylococcus aureus* and *albus* and, less frequently, the *Streptococcus* and the *Pneumococcus* were found to be the offending organisms. Expectant treatment seems to be indicated at first, especially if one bears in mind those cases in which operation has led to a lesion of the pleura and empyema. The prognosis is favorable except when it is associated with a generalized septicemia. Poulsson reports three cases of non-specific osteitis, with a number of roentgenograms illustrating the roentgenographic picture of the disease.

G. E. BURCH, M.D.

BONE DISEASES (THERAPY)

Roentgen Therapy of Hand-Schüller-Christian's Disease. R. Glauner. Strahlentherapie, 1937, **60,** 58.

The author reports a case of Hand-Schüller-Christian's disease with involvement of the skull and upper left femur. There was also destruction of the sella turcica, with exophthalmos. Roentgen therapy was given to the skull through three areas: 180 r, 120 r, and 180 r were applied over these areas so that during a three-week period the total surface dose amounted to 1,020 r. A total surface dose of 1,080 r through two areas was given to the upper left femur. During that time a new lesion appeared in the right upper tibia. This received a total surface dose of 720 r. The bone lesions improved after the treatment, as well as the exophthalmos. Further treatment was given one month later. Six months after the last series there was complete healing of all bone lesions. The child had developed normally and no new lesions had appeared. The author points out that apparently high doses are required; in his case, for instance, 2,100 r to the skull and 2,280 r to the upper thigh. The response of this disease to roentgen rays can well be explained by the histological character of the lipoid granulomatous tissue.

ERNST A. POHLE, M.D., Ph.D.

Osseous Echinococcosis. E. Ettorre. Arch. ital. di chir., January, 1937, **45,** 149–174. (Reprinted by permission from British Med. Jour., May 22, 1937, p. 81 of Epitome of Current Medical Literature.)

The author, who records a personal case of echinococcus disease of the scapula, states that localization of the disease in bone is rare, as Ivanissevitch, among 1,734 cases of echinococcus disease notified in the Argentine Republic, found only 29 cases (1.6 per cent) in which a bone was involved. Ettorre could collect only eight cases beside his own in which the scapula was affected. His patient was a woman aged 28, a native of Milan, who at the age of 12 had received a violent blow on her left shoulder. About three years later she began to feel pain in the shoulder, which was attributed to pleurisy and treated as such. During the last three years pain was felt in movements of the shoulder, especially on abduction and internal rotation, and a diagnosis of arthritis was made. Shortly afterwards a swelling appeared, gradually increasing in size. As the result of radiological examination and exploratory puncture a diagnosis of echinococcus disease of the scapula was made and the cysts successfully removed. Complete recovery took place.

BONES, TUMORS

Osteochondromatosis of the Tibio-tarsal Articulation. J. Prouzet and Reberol. Bull. et Mém. Soc. Radiol. Méd. de France, January, 1937, **25,** 93, 94.

Osteochondromatosis of the ankle joint is a rare condition, the authors finding but three recorded cases. Their case, a man 25 years of age, had sprained his ankle six years previously. This was treated by rest and massage. Subsequently massage relieved him of an occasional recurrence of swelling and pain. The x-ray showed a mass of small calcified bodies of indefinite outline anterior and posterior to an otherwise quite normal ankle joint. A second film, six months later, showed decrease in number of the smaller osteophytes.

S. RICHARD BEATTY, M.D.

A Case of Bilateral Articular Chondromatosis. Serrand and Bertreaux. Bull. et Mém. Soc. Radiol. Méd. de France, February, 1937, **25,** 114, 115.

A case of bilateral chondromatosis of the elbows is presented, interesting also in that there were deformities of the radius and ulna due to osteophytes in the region of the articular margins.

S. RICHARD BEATTY, M.D.

THE BRAIN

Problem of Post-operative Irradiation in Brain Tumors (Clinical Part, L. Guttmann, Strahlentherapie, 1937, **59,** 316: Roentgen Part, C. Fried, ibid., p. 328).

The first paper deals with the clinical and surgical aspect of brain tumors while the second paper contains the report of the roentgenologist. The author uses 180 kv., 4 ma., 0.5 mm. Cu + 1 mm. Al, 40 cm. F. S. D.,

6 × 8 sq. cm. As many areas as feasible were irradicated, as a rule four or five small areas. The doses applied fluctuated considerably; beginning with 400–500 r, the total doses reached in some patients over 32,000 r. In a few instances the method of Wintz and Holfelder was employed giving in from eight to ten days about 2,000 r total surface dose. The end-results are tabulated, offering also a brief analysis of the clinical data for each patient. The best results are apparently to be expected from a combination of operation and irradiation. Partial removal of the tumor should be followed by courses of intensive radiation therapy.

ERNST A. POHLE, M.D., Ph.D.

BREAST CANCER

The Post-operative Irradiation of Cancer of the Breast. H. Bade and K. Baden. Strahlentherapie, 1937, **60,** 189.

The authors describe the method developed by Meyer in the post-operative irradiation of carcinoma of the breast. Moderate doses are used, being given over a two-year period following operation at increasing intervals. Ten to twelve series of 50–60 per cent H.E.D. are administered. During the period from 1921 to 1933 a total of 105 cases were treated; 43 of these were in Stage I, 42 in Stage II, and 20 in Stage III. The respective percentages of five-year survivals were 65.3, 35.7, and 10 per cent, or a total of 42.8 per cent for all treated cases. In conclusion, the authors stress the importance of close co-operation of surgeon, pathologist, and radiologist.

ERNST A. POHLE, M.D., Ph.D.

CANCER (DIAGNOSIS)

The Problem of "Cancer Families." R. Werner. Strahlentherapie, 1937, **60,** 184.

The author analyzes 15 "cancer families" and found that among 104 members, 58 developed cancer. Cancer of the stomach showed the highest incidence.

ERNST A. POHLE, M.D., Ph.D.

CANCER (THERAPY)

The Results of Several Years' Roentgen Therapy with Small Focal Skin Distance in Carcinoma of the Skin and Lip. H. Chaoul, K. Greineder, and H. Oeser. Strahlentherapie, 1937, **60,** 239.

The authors' method of applying roentgen rays of moderate potential, fairly heavy filter, at very short focal distance has been described repeatedly. In this article they relate the results obtained with this method during the last three years. They treated 171 skin cancers; 85.3 per cent have remained well over a three-year period. The percentage for 42 cases with cancer of the lip was 83.3 per cent. They also quote several other investigators who report similar results with this method. The doses applied varied from 5,000 to 10,000 r. In conclusion, the authors state that this method of roentgen therapy compares well with radium.

ERNST A. POHLE, M.D., Ph.D.

The Co-operation of the Hospital in the Fight against Cancer. H. Holthusen and A. Hamann. Strahlentherapie, 1937, **60,** 70.

This is a statistical analysis of the patients admitted to the St. George Hospital, in Hamburg, with the diagnosis of tumor during the period from 1931 to 1935. The tabulations show the distribution of the tumors as to localization, morbidity statistics, the type of treatment received in the hospital, and the age distribution. The operation of the social service division is also discussed.

ERNST A. POHLE, M.D., Ph.D.

DIATHERMY

The Qualitative and Quantitative Differences in the Radiation Emitted between Natural Sun and Therapeutic Lamps: Description of a New Lamp Emitting Practically the Same Spectrum as the Sun. E. Witte. Strahlentherapie, 1937, **58,** 113.

The author describes briefly an aritificial source of light the spectrum of which approaches that of the sun, especially if combined with a quartz mercury vapor lamp filtered through uviol glass. The latter removes ultra-violet rays below 2,700 Å. The lamp consists of five nitraphot glow bulbs of 500 watts each. It uses a water filter of 1 cm. thickness, so cooled as to keep its temperature always under 40° C. In a short paragraph some of the preliminary clinical observations are described.

ERNST A. POHLE, M.D., Ph.D.

DOSAGE

Influence on the Biologic Object of Rhythmic Interruption of Roentgen Irradiation. P. Zacharias. Strahlentherapie, 1937, **59,** 224.

The author exposed seedlings of *Vicia faba equina* to roentgen rays, using the protracted fractional dose method and exposure interrupted at regular intervals. His apparatus allowed 10 seconds of irradiation followed each time by 20 seconds at rest. This type of application seems to be better tolerated than continuous irradiation, provided, of course, that in both instances the same total time was used.

ERNST A. POHLE, M.D., Ph.D.

THE EAR (MIDDLE)

Cholesteatoma in Chronic Otitis Media. A. S. MacMillan. Am. Jour. Roentgenol. and Rad. Ther., December, 1936, **36,** 747–750.

The fronto-occipital position is advocated for showing the smooth rounded and multiloculated cavities occurring in the middle ear, attic, or mastoid antrum, with the Law mastoid projection also being employed to aid in differentiating large emissary veins and deep lateral sinus grooves. The density of the cholesteatoma, compared with the surrounding dense bone, is negligible, hence films taken after operative removal of the cholesteatoma will present the same appearance as before removal. The average size of the mastoid

antrum in the completely sclerosed mastoid measures 6 mm. transversely by 10 mm. vertically; an increase in size beyond these limits may be attributed to eroding cholesteatomas.

J. E. HABBE, M.D.

ENCEPHALOGRAPHY

Tumor of the Brain, with Normal Encephalogram. Nathan Savitsky and Morris B. Bender. Am. Jour. Med. Sci., July, 1937, **194,** 96–103.

In a series of 500 tumors of the brain these authors found 120 patients with intracranial air injections; seven showed normal aerograms. These, with two other cases, constitute the basis for the present report. The series indicates that brain tumors, irrespective of their location, nature, size, and rate of growth, may exist for a long time without significant alterations in the ventricular and subarachnoid spaces. Of the nine cases reported, tumors were found in the parietal lobe in three, in the frontal lobe in four, and in the corpus striatum and temporal lobe in one, and in the basal ganglia in one. The duration of the course of the disease varied from two months up to 19 years, until the time a normal encephalogram was found. In four instances, papilledema was present.

Emphasis is placed upon the facts that during earlier stages of a brain tumor the aerograms may be negative, that normal ventricular and subarachnoid systems may exist irrespective of the nature and location of the tumor and the duration of its course, and that a negative encephalogram does not exclude the diagnosis of a tumor based on clinical grounds.

W. A. SODEMAN, M.D.

THE ESOPHAGUS

Narrowing of the Inferior Esophagus as a Clinical Entity. A. Soulas. Arch. d. mal. de l'app. digestif, March, 1937, **27,** 299–313.

A. Soulas discusses the narrowing of the esophagus at the cardio-esophageal junction. He believes such narrowings can be classed as accompaniments of megaesophagus due to hypertrophy of the sphincter, or as stenosing inflammation of the musoca muscularis extending to the mucosa and accompanied by inflammatory edema and purulent exudate with later fibrosis.

He cites the symptomatology and the clinical, radiologic, and esophagoscopic findings in a number of cases and discusses the therapy.

S. RICHARD BEATTY, M.D.

Cancer of the Esophagus Treated by Deep X-ray Therapy. Herbert Tilley. British Med. Jour., June, 1937, pp. 1199, 1200.

This case report describes a patient with cancer of the mid-third of the esophagus treated by a technic permitting entry of the rays through six long narrow fields centered over the esophagus. Such a method, the author states, produces good palliative results in over 60 per cent of the cases. The mid-third growths do very well for a time, a year or two, but death ensues within two and a half years.

In the present case the patient lived two years and eight months and was entirely symptom-free for one year and eight months, with little difficulty for a further period of eight months.

W. A. SODEMAN, M.D.

GALL BLADDER (NORMAL AND PATHOLOGIC)

The Influence of Extra-biliary Disease on the Function of the Gall Bladder: A Cholecystographic Study. C. Allen Good, Jr., and B. R. Kirklin. Am. Jour. Roentgenol. and Rad. Ther., March, 1937, **37,** 346–349.

In 733 patients with diagnoses such as peptic ulcer, pernicious anemia, thyrotoxicosis, myxedema, diabetes mellitus, obesity, pulmonary tuberculosis, or chronic appendix, the gall bladder was examined with the oral dye. In 167, that organ was found functioning poorly or not at all. Of those, 106 were examined by operation or at autopsy and 104 were found to be diseased, thus proving that extra-biliary diseases have little or no influence on the cholecystographic function of the gall bladder.

S. M. ATKINS, M.D.

Cholecystography: The Efficiency of the Graham-Cole Test. T. Garratt Hardman. British Med. Jour., Oct. 16, 1937, pp. 733, 734.

Hardman found in his cases that the oral method of cholecystography indicated in 90 per cent of the cases whether the gall bladder was normal or pathological. The fact that 10 per cent of errors may occur is good reason for urging that the Graham-Cole test should not be used to supplant the usual clinical methods of examination but should take its place as part of the ordinary routine investigation as a valuable aid in the diagnosis of cholecystic disease. The success of the method depends upon the most careful attention to detail in preparation and to correct radiographic technic.

G. E. BURCH, M.D.

GASTRO-INTESTINAL TRACT (DIAGNOSIS)

Chronic, Non-specific Regional Ileocolitis. C. J. Hansson. Acta Radiologica, August, 1937, **18,** 635–642.

Hansson discusses the clinical and pathological picture of regional ileocolitis. Roentgenologically he finds with the aid of contrast lavages, a normal mucous membrane of the colon instead of an absence of the mucous-membrane relief characteristic of colitis. However, in more advanced cases alterations may be observed in the cecum and may even extend up the ascending colon. The alterations are characterized by a smooth, cornet-shaped constriction of the lumen down to the valve of Bauhini. The alterations may be of such a degree that the lumen becomes as narrow as a string, often referred to as the "string sign" in American literature. The

narrowing is produced by infiltration of the intestinal wall, which progressively diminishes as it extends up the ascending colon. The intestine is smooth in contour. The valve of Bauhini is constricted, thus frequently making it difficult to determine where the ileum ends and the colon begins. It is also difficult to force the contrast medium past the colon into the ileum. Infiltration of the wall of the terminal portion of the ileum and cornet-shaped stenosis toward the valve of Bauhini are observed, embracing about the terminal 15 to 20 cm. of the ileum. In this altered area, one palpates a tender tumor and a fixed or slightly displaceable intestine. On passage examination, one usually observes dilation of the healthy intestine above the altered area together with slowing down of the passage through the small intestine.

G. E. Burch, M.D.

Diverticula of the Digestive Tract. Friedrich Umber. München. med. Wchnschr., Aug. 27, 1937, **84,** 1377.

A rather brief monographic exposition of the symptoms, diagnosis, treatment, and prognosis of traction and pulsion diverticula of the esophagus, diverticula of the stomach and duodenum, of the colon, and Meckel's diverticula. No new material is presented. The article is illustrated and case reports amplify the descriptions.

Lewis G. Jacobs, M.D.

Discussion on Some of the Less Common Lesions and Special Methods of Investigation of the Alimentary Tract and the Influence of Adjacent Organs. C. Gage, S. C. Shanks, R. S. Paterson, and G. Bush. Proc. Royal Soc. Med., September, 1937, **30,** 1371–1392.

The subjects of the symposium are briefly discussed and include the salient roentgenographic features of the diseases which aid in diagnosis. The conditions presented were sarcoma of the stomach, polyposis of the stomach, retroperitoneal hernias, primary carcinoma of the duodenum, Crohn's disease, and *Ascaris lumbricoides*. Unusual methods of examining the pharynx, esophagus, stomach, pancreas, small intestine, and colon; roentgenologic examination and features in diseases of the colon, and the influence of adjacent organs and tumors on the alimentary tract are also discussed.

G. E. Burch, M.D.

GENITO-URINARY TRACT (DIAGNOSIS)

Congenital Abnormalities in the Urinary Tract of a Six-year-old Child. M. Bernasconi. Bull. et Mém. Soc. Radiol. Méd. de France, February, 1937, **25,** 154, 155.

The author reports a case of a child six years of age who had a right-sided mega-ureter with hydronephrosis and vesico-renal reflux on the left, despite a normal ureteral orifice. The position of the pelves and ureters led to the diagnosis of horse-shoe kidney.

S. Richard Beatty, M.D.

GENITO-URINARY TRACT (THERAPY)

Effect of Various Wave Lengths on the Aschheim-Zondek-Friedmann Reactions. T. M. Caffaratto and M. Bertini. Strahlentherapie, 1937, **59,** 276.

The authors studied the effect of infra-red rays, ultra-violet rays, and roentgen rays (170 kv., 3 ma., 30 cm. F.S.D., 1 mm. Al, 300–3,600 r) on the Aschheim-Zondek-Friedmann reaction. Urine of pregnant women at the beginning and end of the pregnancy was used. They found that the reaction was more pronounced if the urine had been exposed to the roentgen and infra-red rays, while ultra-violet rays seemed to depress it. From a practical standpoint they suggest irradiating the urine specimen since the reaction is not only more pronounced but occurs sooner than under ordinary conditions—in many instances as early as 24 hours after the injection.

Ernst A. Pohle, M.D., Ph.D.